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SURGERY OF THE SPLEEN

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BY

EUGENE H. POOL, M.D.

ATTENDING SURGEON, NEW YORK HOSPITAL; CLINICAL
PROFESSOR OF SURGERY, COLUMBIA UNIVERSITY

AND

RALPH G. STILLMAN, M.D.

CLINICAL PATHOLOGIST, NEW YORK HOSPITAL; ASSISTANT PROFESSOR
OF CLINICAL PATHOLOGY, CORNELL MEDICAL SCHOOL

SURGICAL MONOGRAPHS

UNDER THE EDITORIAL SUPERVISION OF

DEAN LEWIS, A.B., M.D.

PROFESSOR OF SURGERY, RUSH MEDICAL COLLEGE

EUGENE H. POOL, A.B., M.D.

ATTENDING SURGEON, NEW YORK HOSPITAL

ARTHUR W. ELTING, A.B., M.D.

PROFESSOR OF SURGERY, ALBANY MEDICAL COLLEGE



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PREFACE

It has long been recognized that American contributors to medical literature have not followed the monographic form to the same degree as European writers. This deficiency has proved a handicap to English speaking students.

The interference during the War with foreign research and publications emphasized this feature, since there was an abrupt arrest of the usual stream of exhaustive and desirable articles from foreign sources. After the War, American surgeons recognized that the time was appropriate to encourage a more general adoption of the monographic form for surgical contributions. The ideal was often expressed that the American reader might soon have access to a wide range of surgical subjects exhaustively treated. The editors of this series have attempted to fill this need, and the assignment of the spleen to the writers explains this volume. The subject is presented with a full knowledge of its limitations and deficiencies, but in the hope that together with the other volumes of this initial set it will constitute a beginning of an ever increasing and ever improving group of surgical monographs by American authors.

The writers are under obligation to Dr. F. Robbins and Dr. H. C. Falk, for assistance in reviewing the literature, and to Dr. William Elser of the New York Hospital, for much help in the preparation of the parts which bear upon pathology, especially the consideration of neoplasms of the spleen.

E. H. P.

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SURGERY OF THE SPLEEN

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CHAPTER I

INTRODUCTION

OF all the structures in the body, the spleen preëminently deserves the name of organ of mystery. It is large in size, the largest aggregation in the body of its particular type of tissue. It contains no epithelial tissue and no duct. No peculiar secretion nor function has been found to dignify this organ as one of the physiological forces of the body. It has intimate circulatory relations with the liver and gastrointestinal tract, yet no physiological significance has been shown to be dependent upon this association. The contents of the splenic vein pass through the liver and therefore materials added to the blood in the spleen may exert an influence upon the liver. But the liver can exercise no influence upon the spleen, more than upon any other organ, except in the production of such changes as may result from obstruction to the portal circulation. The spleen, except in certain infections, is not affected by changes in the stomach or intestines nor are the latter directly influenced by changes in the spleen. Yet one must bear in mind the possibility that the spleen may contribute some substance to the portal circulation which, mixing with the blood from the stomach and intestines, may neutralize or combine with substances, possibly toxic in nature, elaborated therein.

Every other organ in the body, with the exception of those which are undergoing retrograde changes, has been shown to have some special function; the spleen alone is dispensable. Its removal seems to result in no permanent changes in body chemistry or physiology. Even in disease its influence is not readily distinguishable. In those conditions in which the spleen is conspicuously involved, symptoms may be ascribed, as a rule, to mechanical causes or traced to the involvement of other organs. Its capacity for enlargement and the readiness with which the large spleen produces disturbances mechanically have attracted to it the attention that is always received by the obvious. Even in a consideration of the clinical improvement which not infrequently follows the removal of an enlarged spleen, it is often possible to construct a plausible hypothesis in which this organ occupies a position of secondary importance. Yet the size, permanence and vascular relations of the spleen are such that we do not feel justified in passing it by as merely the largest lymph-node in the body. Its prompt, and

in some respects specific, reaction to some infections and its failure to respond to others suggests that it may have an important function in certain of the infectious diseases.

The development of the surgery of the spleen has been slow and has taken place for the most part in comparatively recent years. Because this organ is relatively inaccessible, its physiological activity for the most part unknown, and evidences of its malfunction obscure, surgeons long failed to recognize that it might belong to their domain. Its surgery received its initial impulse when it became evident that no injurious effects resulted from the removal of the organ for wounds; its removal for splenomegaly followed, and finally for certain of the blood diseases.

It is in connection with this last group, diseases of the blood, that the main interest in the organ for the surgeon is centered. Successful surgery in these conditions requires detailed analysis of the various diseases of the blood which are associated with splenomegaly and careful study of the production of the blood. Yet the surgery of the spleen at present is largely empirical, based chiefly upon hypotheses and the observation of patients after operation.

Historical.—It is of interest to note that reference to the spleen dates well back into the earliest days of the science of medicine. Sobotta is authority for the following brief historical outline.

A description of the organ is found in the writings of Aristotle, and mention of the spleen is made by several others of the older writers, such as Rufus Ephesius, Aretaeus, Paulus Aegineta, and especially by Galen, who believed the organ to be connected with the liver. This statement was corrected by Vesalius. In the latter part of the sixteenth century, Franciscus Ulmus published a treatise on the spleen, which he included under the heading of the vascular system. The increasing number of publications on the spleen in the seventeenth century were chiefly of a physiological character. A detailed description of the spleen is found in the works of Highmore. Glisson's monograph on the liver also contains a description of the spleen. The works of Wharton and of Schenk likewise deal with this organ.

The greatest credit for the investigation of the spleen in the seventeenth century belongs to Marcello Malpighi, who discovered and described the splenic follicles known after him as malpighian corpuscles, though he remained unaware of the finer structure of these bodies. Malpighi was the first to claim an internal secretion for the spleen; the veins were supposed to receive the secretion, instead of excretory ducts. Ruysch was the first to rank the spleen with the thyroid, the suprarenals and the lymph-nodes. The name of "*glandulae sanguineae*," blood-glands, or glands without excretory ducts, was introduced by him. Some additional knowledge of the spleen was furnished by Morgagni (1718).

The first microscopic description of the structure of the spleen is found in Leeuwenhoek's "Microscopical Observations on the Structure of the Spleen." He described the connective tissue, the nonmuscular trabecular framework, and recognized the composition of the organ by minute corpuscular elements, but no mention is made of the malpighian corpuscles. The series of modern descriptions of the splenic structure and its microscopic anatomy begins with the investigations of J. Müller who first described the venous capillaries of the splenic pulp, the behavior of the arteries, and the relations of the malpighian corpuscles with the small arterial branches.

The literature covering the diseases and surgery of the spleen is voluminous. Laspeyres gives a full bibliography from 1894 to 1903, and Michelsson from 1903 to 1913. Chavannaz and Guyot and Mario Segré have recently presented exhaustive analyses of the surgery of the spleen. These works have been freely used in the preparation of this article. Complete bibliographies up to about 1918 are given in these monographs. The literature since that date has been quite fully reviewed and the more important references are appended, together with the bibliography of articles referred to in the text.

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CHAPTER II

THE ANATOMY OF THE SPLEEN: EMBRYOLOGY, ANOMALIES AND HISTOLOGY

EMBRYOLOGY

The spleen is mesodermal in origin. It arises from a thickening of the left side of the mesogastrium and can be recognized readily in 8 to 10 mm. embryos (about the fifth week). The mesothelium usually consists of a single layer of cells well marked off from the mesenchyma.



FIG. 1.—SECTION THROUGH DORSAL MESOGASTRIUM (ANLAGE OF SPLEEN). (Courtesy Tonkoff. Bailey and Miller, Embryology.)
A chick embryo three days and twenty-one hours' incubation.

In this region, however, the mesothelium for a brief period consists of several layers of cells not so distinctly separated from the mesenchyma. This lasts only for a short time, for in 42-day embryos the mesothelium is again a single layer. As development proceeds, the elevation becomes larger and projects into the body cavity. Its attachment to the mesentery (mesogastrium) becomes smaller and finally forms a narrow band of tissue through which the splenic vessels pass.

Thiel and Downey have recently described as follows the development of the mammalian spleen:

In the substance of the developing spleen the rudiments of the cavernous vessels appear as spaces among the mesenchymal cells. Subsequently the capillary network which is already present establishes communication with these spaces, thus giving the characteristic open circulation of the adult organ. Formation of red blood corpuscles (erythropoiesis) takes place in the mesenchyme among the cavernous vessels, the cells passing into the circulation through the walls of the vessels. Development of the granular forms of white blood cells in the spleen seems to be rather limited in the embryo. The lymphocyte

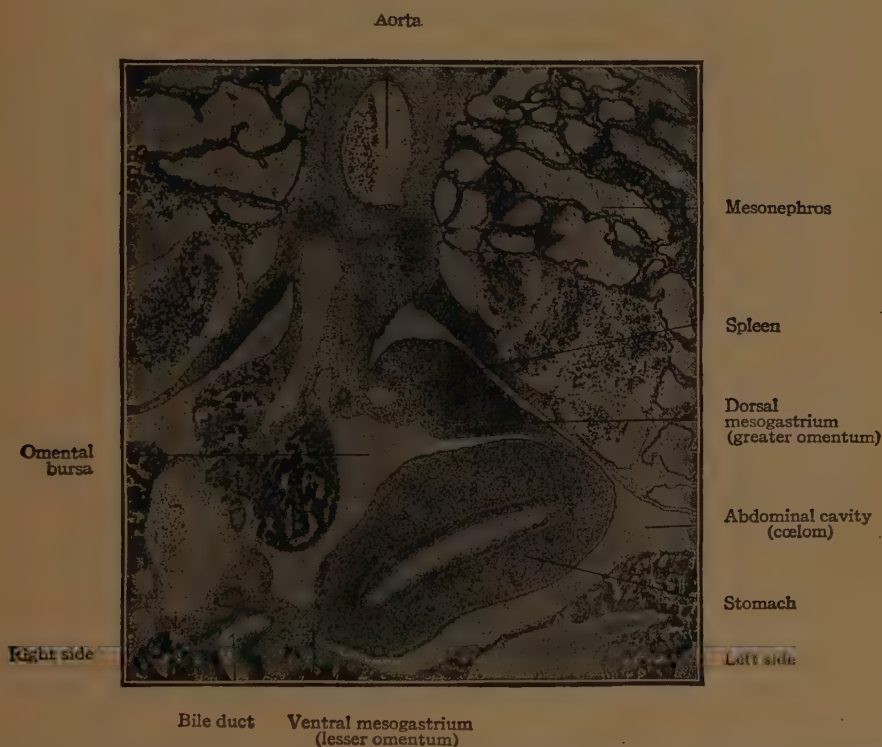


FIG. 2.—TRANSVERSE SECTION THROUGH STOMACH REGION OF 14 M.M. PIG EMBRYO. (Courtesy Bailey and Miller, Embryology.)

series, however, is freely formed in the mesenchyme, and aggregations of these cells in the adventitia of the walls of the arteries give rise to the splenic corpuscles.

Anatomy.—The spleen lies deeply in the most remote and highest portion of the left hypochondrium behind the fundus of the stomach, and is covered by the lower ribs. It is an unpaired, soft, dark bluish red organ of variable size, almost entirely covered by peritoneum.

According to E. Stricker, quoted by Sobotta, the average size of the spleen at various ages is as follows:

	Centimeters
Birth	5 x 3 x 1.7
12 months	7.8 x 4.2 x 2
24 months	6.8 x 3.7 x 1.7
3d year	7.2 x 4.1 x 1.7
4th year	7.6 x 4.3 x 2
5th year	8.3 x 4.7 x 2.2
8th year	8.3 x 5.2 x 2
12th year	10.7 x 6.2 x 2.3
16th year	11.2 x 6.4 x 2.5
18th year	12.7 x 7.2 x 2.8

The last figures are approximately those prevailing throughout adult life.

T. Shennan gives the average size of the adult spleen as 5 inches (11-14 cm.) by 3 inches (7-8 cm.) by 1 inch (2.5-3 cm.). The normal weight he gives as from 5 to 8 ounces (150-250 gm.). In 1,325 autopsies, he found the average weight to be 176 gm. or nearly 6 $\frac{1}{5}$ ounces. In 802 males, the average weight was 184 gm. (6 $\frac{1}{2}$ oz.); in 523 females 159.5 gm. (5 $\frac{1}{2}$ oz.). It is claimed by Blan and Baker that the spleen is smaller in the negro than in the white.

As described by Cunningham and Quain, the organ when hardened *in situ* has the shape of an irregular tetrahedron, with its apex above and its base below. The upper extremity, which may be regarded as representing the apex, is directed inwards and upwards, and reaches to within about an inch of the left side of the vertebral column, usually opposite the body of the eleventh dorsal vertebra. Of the four surfaces (diaphragmatic, gastric, renal, and colic or basal), the most extensive is the *diaphragmatic*, which is adapted to the concavity of the diaphragm, corresponding in position to the eighth (Quain), ninth, tenth, and eleventh ribs. The remaining three surfaces are turned towards the cavity of the abdomen, and are closely applied to the neighboring viscera. These three surfaces meet at a blunt but usually very conspicuous prominence, which may be termed the intermediate angle (internal basal angle). From this as a center three ridges radiate. One salient and prominent (margo-intermedius, antero-internal or inner border) ascends to the apex or upper extremity, and separates the gastric from the renal surfaces; a second short ridge passes backward to the posterior angle, and intervenes between the renal and the colic surfaces; while a third ridge, less distinctly marked, proceeds forward to the anterior angle, and separates the gastric and the colic surfaces. The last two mentioned ridges, together with the lower border of the organ, map out a triangular area which may be distinguished as the colic surface. The *gastric* surface, looking forward and inward, is deeply concave and is molded upon the fundus of the stomach. Within its area, about 1 cm. to the outer side of the margo-intermedius, is situated

the hilum of the spleen, "a long fissure or more frequently a series of depressions through which the vessels and nerves enter the spleen, and around which the peritoneum is reflected from the surface of the organ." The *renal* surface is not concave as a rule, but flat and even. It varies considerably in extent, and is applied to the anterior surface of the upper part of the kidney, close to its lateral border. The *colic* surface is smaller than the other two visceral surfaces. It is directed downward and inward, and is in relation with the left colic flexure and the phrenocolic ligament. The area of contact with the pancreas is subject to considerable variation and in many cases a marked pancreatic depres-

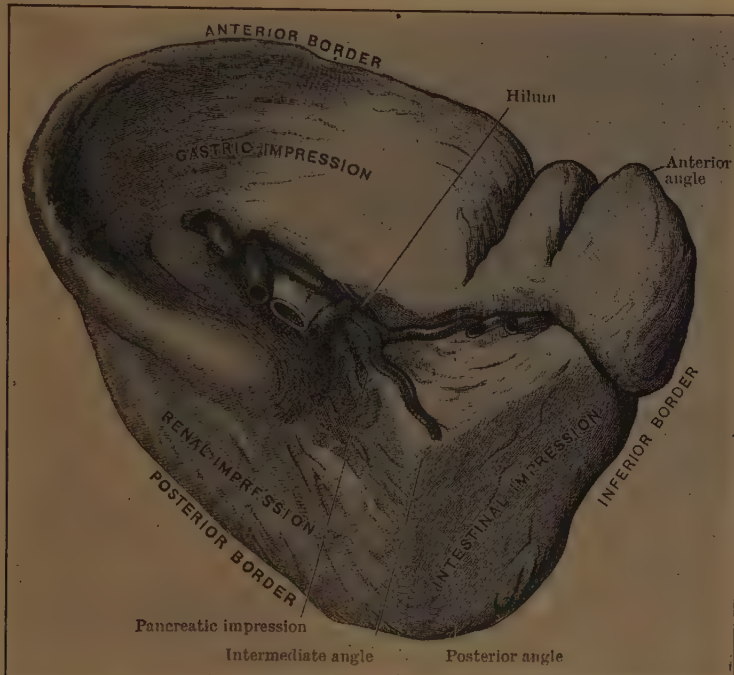


FIG. 3.—THE SPLEEN—VISCERAL ASPECT. (Courtesy Cunningham, Anatomy.)

sion may be observed on the spleen behind the hilum and immediately in front of the intermediate angle.

The spleen presents a well-marked inferior border which stretches from the posterior to the anterior angle, and intervenes between the colic visceral surface and the external diaphragmatic surface. The great prominence of the anterior angle is a characteristic feature of the typically formed spleen, and constitutes a striking projection which appears to be more strongly marked in the fetus than in the adult. It forms the most anteriorly placed part of the organ.

From the anterior angle passing upward to the apex is the anterior border. This is the most prominent; it separates the gastric from the diaphragmatic surfaces and often presents one or two notches near its

lower end. The posterior border intervenes between the diaphragmatic and renal surfaces.

Peritoneal Relations.—The spleen is supported in position by peritoneal attachments termed ligaments. Appreciation of the peritoneal relations of the organ and of these supporting folds is dependent upon a knowledge of their development. Huntington, in his monumental work on the human peritoneum, summarizes the peritoneal development in this region as follows:

The spleen develops from the mesoderm between the layers of the dorsal mesogastrium, near its point of accession to the greater curva-

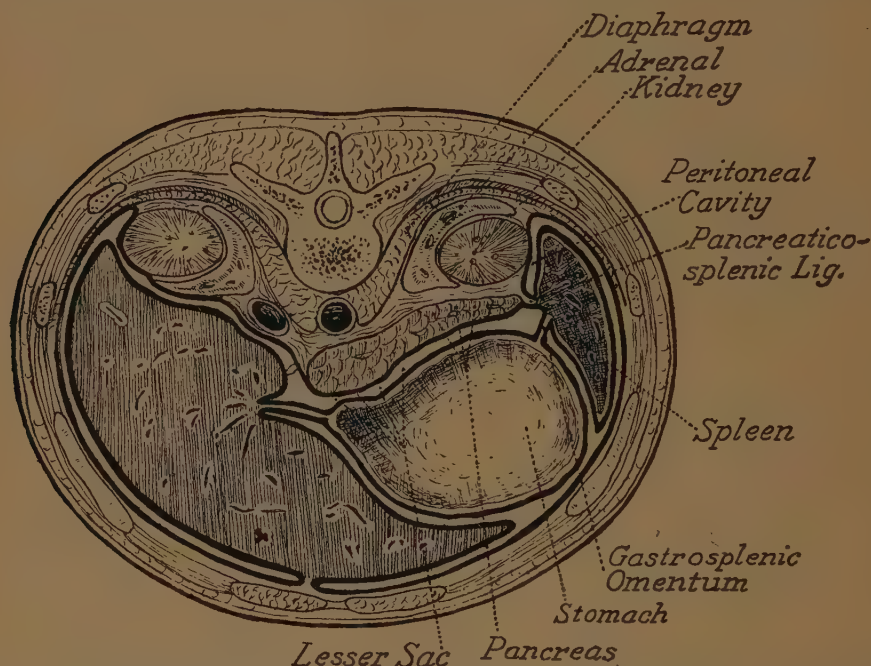


FIG. 4.—TRANSVERSE SECTION AT LEVEL OF TWELFTH DORSAL VERTEBRA. (Adapted from Sobotta.)

ture of the stomach, in the region of the subsequent fundus. After rotation of the stomach, the organ (spleen) lies between the two layers of the membrane at the extreme left end of the retrogastric space. Through the development of the spleen the dorsal mesogastrium has been subdivided into a proximal, longer, vertebrosplenic and a distal, shorter, gastrosplenic segment (*gastrosplenic ligament*). The former loses its identity as a free membrane in the human adult by fusing with the parietal peritoneum investing the ventral surface of the left kidney. The lateral limit of the area of adhesion between mesogastrium and parietal peritoneum is situated along the lateral border of the left kidney. Hence, in the final condition of the parts, the main splenic vessels at the hilum are situated between two peritoneal layers of which the ventral appears as the parietal peritoneum, forming the dorsal wall

of the retrogastric space, while the dorsal layer forms a reflection from the mesial surface of the spleen, along the dorsal margin of the hilum, to the adjacent lateral border of the left kidney (*lienorenal ligament*) and to the diaphragm. At this point of adhesion firmer strands of con-



FIG. 5.—SCHEMATIC TRANSVERSE SECTION OF THE ABDOMEN. (Courtesy Huntington, Anatomy.)

This shows early stage of development of the spleen from extreme left of dorsal mesogastric pouch.

nective tissue subsequently develop in the serous reduplication forming the *ligamentum phrenicocolienale* of systemic anatomy.

A connection with the colon produced by adhesion of the mesogastrium to the splenic flexure of the large intestine forms the adult *ligamentum colicocolienale*, while a similar adhesion between great omen-

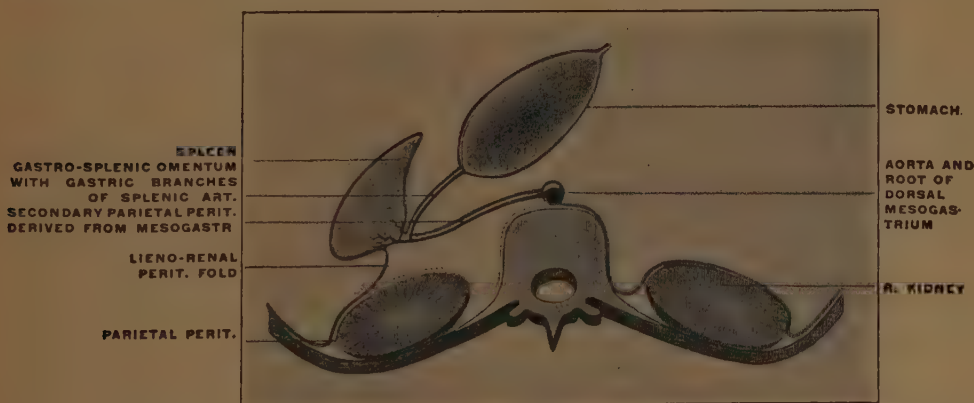


FIG. 6.—SCHEMATIC TRANSVERSE SECTION OF ABDOMEN. (Courtesy Huntington, Anatomy.)

This shows later stage of development of spleen and arrangement of peritoneum after adhesion of dorsal layer of mesogastrium and primitive parietal peritoneum.

tum, transverse mesocolon and phrenic parietal peritoneum just caudad of the spleen gives rise to the *colicophrenic* or *costocolic* supporting ligament of the spleen.

In Fig. VII (Huntington, Fig. 183) the spleen of a child two years of age has been removed from the preparation by division of its peri-

toneal and vascular connections and is shown in its mesial aspect. It will be seen that the peritoneal reflections are arranged in the form of concentric, elliptical lines. The two ventral lines form the gastro-splenic omentum and correspond to the reflection of the peritoneum from the spleen to the left end of the stomach carrying the gastric branches derived from the splenic artery. The third line, from before backward, results from the division of the secondary parietal peritoneum of the lesser sac, covering the splenic artery, and ventral surface of the pancreas, while the most dorsal fourth line represents the divided reflection of the peritoneum from the renal surface of the spleen, to the lateral border of the left kidney and diaphragm (*ligamentum lienorenale*).

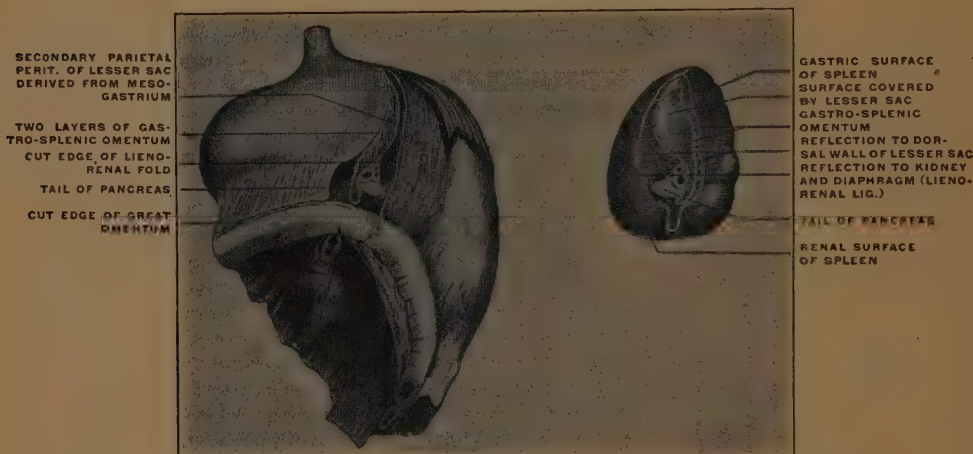


FIG. 7.—SPLEEN REMOVED. (Courtesy Huntington, Anatomy.)

This shows lines of peritoneal reflection on mesial surface of the organ.

Between the second and third lines of the peritoneal reflection appears the mesial surface of the spleen in contact with, and invested by, the extreme left end of the lesser peritoneal sac.

The peritoneal ligaments of the spleen are:

Gastrosplenic ligament, composed of two layers of peritoneum, the anterior of which is derived from the greater sac, while the posterior is derived from the lesser sac. It connects the gastric surface of the spleen with the greater curvature of the stomach.

Lienorenal ligament, composed of two layers which inclose the main splenic vessels. The anterior of these two layers is the posterior layer of the parietal peritoneum of the lesser sac reflected to the spleen. The posterior layer is the peritoneal reflection from the spleen to the lateral border of the left kidney.

Phrenicocolic ligament, a reduplication of peritoneum extending to the diaphragm above the lienorenal ligament. It is formed from the upward extension of the peritoneal layer which constitutes the posterior layer of the lienorenal ligament.

Colocolienal ligament, a reduplication which passes from the spleen to the splenic flexure of the colon. It is practically the lower extension of the lienorenal ligament.

Phrenicocolic ligament, a firm dense fold of peritoneum which connects the splenic flexure of the colon with the diaphragm at the level of the eleventh rib in the midaxillary line. This ligament in the upright position of the body holds the spleen as in a sling.

Pancreaticolienal ligament, described by Sobotta as the lower part of the lienorenal ligament.

Blood Supply.—The *splenic artery*, the largest branch of the celiac axis, supplies the spleen. It passes along the upper border of the pancreas, across the front of the left kidney to the spleen.

Pigache and Worms, on examining the course and distribution of the splenic artery in 32 subjects, found that its branches to the hilum of the spleen were fairly constant. These are the artery to the superior pole, the superior and the inferior terminal branches.

The artery to the superior pole was found in 21 of the 32 cases examined. It arises from the splenic artery 5 to 6 cm. from the spleen, and approaches the hilum obliquely. It is the most superior vessel at the hilum of the spleen. Occasionally it gives off a branch to the greater curvature of the stomach. Near the gland it divides into two or three branches.

The superior and inferior terminal branches represent the termination of the splenic artery. They approach the hilum and, when close to the gland, break up into many smaller vessels which enter the organ and supply the inferior pole. The left gastro-epiploic occasionally arises from the inferior of the two terminal branches, and vasa brevia, three to seven in number, to the greater curvature of the stomach, arise from both the terminal branches.

It is of interest to note that in the development of the spleen the left gastro-epiploic artery is the main vessel and the splenic artery is a branch of it; but as the spleen grows in size the vessel between the celiac axis and the spleen enlarges, and the left gastro-epiploic becomes a branch of the splenic. It courses through the gastrosplenic ligament to the greater curvature of the stomach, taking its origin either from the main vessel 3 or 4 cm. from the spleen or (in 11 of 32 cases) from the inferior terminal branch of the splenic artery.

Veins.—At the hilum, the veins are usually six to eight in number and accompany the arteries. They unite and form a large straight trunk in contradistinction to the tortuous artery. The vein lies below the artery and behind the superior edge of the pancreas and joins the superior mesenteric vein, contributing to the formation of the portal vein.

Lymphatics.—The distribution of the lymph vessels in the spleen has not been determined, but the evidence suggests that the splenic parenchyma itself is devoid of lymphatics. The statement of Sappey, to the

effect that the human spleen has no superficial but only deep lymph vessels, is hardly tenable. Poirier and Cunéo state that "the superficial collecting trunks which were observed by Mascagni, and then by Robin and Legros, are very difficult to inject in man. They are, on the contrary, well developed in the ox and horse. In these animals they form a rich network, which is situated between the peritoneum and the fibrous capsule of the spleen. They then run towards the hilum of the spleen and terminate in the same way as the deep collecting trunks. The deep collecting trunks, which are connected to the preceding by numerous anastomoses, are satellites of the blood-vessels. In the hilum they are reduced to form six to ten trunks which end in the glands of the splenic chain."

The so-called lymphoglandulae pancreaticolienals, as described by Krause, are eight to ten in number and are situated at the hilum of the spleen and along the splenic artery and vein. They probably drain the spleen, a portion of the fundus of the stomach, and part of the body and tail of the pancreas. Poirier and Cunéo state that there are no nodes in the gastrosplenic omentum. Those reported in that situation, they state, are probably accessory spleens.

Nerves.—The nerve trunks of the spleen are exclusively nonmedullated nerve fibers, derived from the celiac plexus of the sympathetic. They form a complicated network around the splenic artery, entering the hilum of the spleen together with the branches of the artery. The behavior of the nerve ramifications in the spleen itself is fairly well known; they are vascular sympathetic branches which follow the course of the arteries. The bulk of the nerve fibers pass to the smooth muscle tissue of the vascular walls, the trabeculae and the capsule (Sobotta).

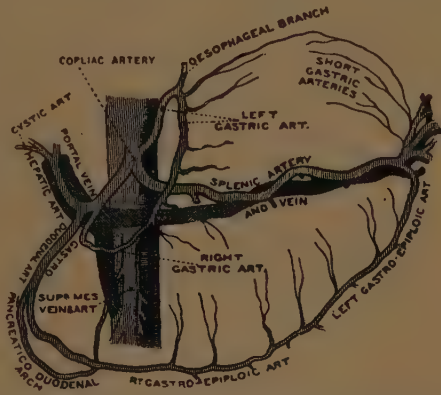


FIG. 9.—CELIAC ARTERY AND ITS BRANCHES.
(Courtesy Cunningham, Practical Anatomy.)

ANOMALIES

Absence of the Spleen.—Complete absence of the spleen occurs rarely, but is compatible with health and longevity. The condition is usually associated with other abnormalities but may occur in otherwise normal individuals. Sternberg, in reporting a case of congenital absence of the spleen in a woman of seventy-three years who died of pulmonary tuberculosis, comments upon the total absence of this organ, while all the other abdominal viscera were normally developed and situated; the arrangement of the splenic artery indicated that the spleen had failed to

develop in embryonic life. Such cases are extremely rare. Hodenpyl reported the case of a colored man thirty-two years of age, who died of obstruction of the common bile duct. At autopsy, no trace of the spleen was discovered. Glinski found no spleen at the autopsy of a woman forty-five years of age, who had died of pulmonary tuberculosis. McLean and Craig have recently reported a case in a child of three months, and have collected and reviewed the previously reported cases.

Microsplenia has been observed in a few cases. Léri, in 1903, found at autopsy a very small spleen weighing only 21 gm. in a man seventy-three years of age which apparently was not due to senile atrophy.

Kuhn reported a normally shaped spleen measuring 3.5 by 2 by 1 cm. in a vigorous man of sixty-four. Paulesco's case was a woman of thirty who died of pulmonary tuberculosis. Her spleen was a rudimentary organ consisting almost entirely of fibrous tissue. Calvert reported a small spleen 32 by 10 by 9 mm. weighing 2.1 gm. in a Filipino woman about thirty years of age, in whom no other abnormalities were found.

Accessory or Multiple Spleens.—Occasionally multiple or accessory spleens are present, that is, small masses of splenic tissue receiving independent vascular branches. Adami and Nichols state that accessory spleens occur in 11 per cent of all autopsies. It is generally thought that they are more common in early life. Jolly reports finding 20 cases with accessory spleens among 80 autopsies on children under sixteen years of age. These accessory spleens are usually encountered, according to Rocher, at the hilum of the spleen, in the gastrosplenic omentum in the "pancreaticosplenic ligament," and in the greater omentum. In the pancreas, occasionally one or more rudimentary spleens of variable size are found. The size of accessory spleens varies from a few millimeters to several centimeters in diameter. They present the same histological structure, and are subject to the same pathological alterations as the main organ. Usually there are not more than one or two accessory spleens, but as many as thirty or forty have been found (Hyrtl).

Albrecht reports a unique case in which there were about four hundred accessory spleens (*splenunculi*) scattered throughout the abdominal cavity, in a man of twenty-five who had been in good health until three months before death from nephritis. There was found at autopsy almost complete absence of the left kidney, malformation of the omentum, and a multiplicity of the spleens (400). The real spleen itself was situated higher than normal and was adherent to the diaphragm by peritoneal folds. This association of multiple spleens with malformations of other viscera is frequent. Hyrtl reports 4 cases of transposition of the viscera, and in every instance he found the spleen broken up into small spleens, five to eleven in number. Of his cases, 2 were newborn and 2 were adults. Garrod reports 2 cases of heart disease with multiple spleens, four and nine respectively. Helly reports a specimen of bilobular spleen with eleven accessory spleens, which is preserved in the Anatomical Institute in Vienna. The spleen is divided by a

groove into two segments joined by connective tissue strands which lodge the ramifications of the splenic artery. This groove passes longitudinally through the hilum of the organ. Eleven accessory spleens, varying in size from that of a lentil to a hazelnut, are attached to both segments as well as to the branches of the splenic artery. By placing the two main parts together, the divided spleen could be made to approach the size and shape of a normal organ.

It is possible for multiple accessory spleens to develop after splenectomy when at the time of operation none were recognizable. It has been thought that these may develop as implantations from particles of splenic tissue scattered at operation, but it is more probable that they represent small collections of lymphoid cells previously present but not recognizable.

A remarkable case of displaced accessory spleen was published by Sneath. A splenic appendage, connected with the normal spleen by a band containing splenic tissue which arose from the upper part of the "intermediate border" behind the lienorenal ligament, was found adherent to the upper pole of the testicle, almost completely ensheathed by the tunica vaginalis; behind, it was adherent to the spermatic cord. The total length of the tail was 33.4 cm., of which about 14.5 cm. contained visible splenic tissue. The scrotal spleen at the top of the testicle was a nodule measuring 2 cm. by 1 cm., which, on microscopical examination, was found to consist of normal splenic tissue. A retroperitoneal position of the spleen has been reported in a few cases (Strychasski, Ehrich).

Transposition.—In transposition of the abdominal organs, the spleen may lie under the right dome of the diaphragm. Sorge, in 1906, published a comprehensive article on *situs viscerum inversus* in which he discussed the hypotheses as to its etiology, and gave references to 194 cases of total transposition of the abdominal viscera. Some few additional cases have been reported since his contribution and have been collected by Sherk. The condition is not as rare as these figures would indicate for numerous instances that are recognized are not reported. The possibility of transposition of the viscera must be borne in mind in cases of uncertain diagnosis; but the condition can always be recognized if a complete and thoughtful physical examination is made.

An illustrative case came under our observation. The patient was a normally developed boy suffering from acute appendicitis, the appendix being close to the left anterior superior spine. The heart apex beat was behind the fifth right rib, 6.5 cm. from the median line; splenic dullness; upper border at seventh rib, anterior border 1 cm. posterior to a line joining the right sternoclavicular articulation and the tip of the eleventh right rib. The liver dullness extended from the fifth left rib to 1 cm. above the left costal margin; its edge could not be felt. By means of the X-ray, the position of the stomach and large intestine could be accurately mapped out. The long axis of the stomach lay from

right to left; the cecum and ascending colon lay on the left side; the descending colon and sigmoid on the right.

The association of multiple spleens with transposition of the viscera, as described by Hyrtl, has already been mentioned.

HISTOLOGY

The spleen may be thought of as belonging to a group of organs of which the other two members are the lymph-nodes and the hemolymph-nodes. At one extreme in this group, the lymph-nodes receive only lymph and contribute the products of their activity to that fluid. The hemolymph-nodes occupy a middle position and receive both blood and lymph. The spleen receives only blood, with the exception of a very limited lymph supply. In a general way, the structure of all the organs of this group is similar and is not fundamentally complex. But there is still much controversy concerning the minute structure of the spleen and it is but imperfectly understood. In a discussion of the histology of the spleen, it is convenient to consider it under several headings.

Supporting Tissue.—The spleen is held within a layer of the peritoneum which has received the name *tunica serosa*. Within this peritoneal investment, the organ is inclosed by the *tunica albuginea*, a capsule made up chiefly of fibrous connective tissue but containing also elastic fibers and a small amount of smooth muscle. Muscle fibers are found in the splenic capsule in such animals as the cat, the dog and the hog, in larger amounts than in man. From the inner surface of the capsule are given off processes which, with their branches, go to make up the supporting framework of this organ. It is to be noted that these branches do not necessarily become smaller as they divide, as is the case with blood-vessels, but that branches may equal in size or be larger than the stem from which they spring. The larger processes are called septa or trabeculae and together with the capsule they form the so-called capsulotrabecular system.

The trabeculae are similar in structure to the capsule, except that they are rather more richly supplied with elastic and muscle fibers. They divide the spleen roughly into lobes which, in some of the lower animals, are clearly indicated by the surface markings of the organ. From the trabeculae, secondary processes arise which branch and anastomose with one another and divide the lobes into incomplete anastomosing chambers known as lobules. In the periphery of the organ, the arrangement of the lobules is more or less regular and they measure about 1 mm. in diameter. Further branching of the connective tissue framework results in a division of the lobule into about ten smaller compartments called splenic units (Mall). The finest twigs of connective tissue, the terminal branches of the trabecular system, contain no elastic or muscle tissue. They penetrate the interior of the splenic

units and furnish support to the pulp. Sobotta claims that the elastic tissue network found in the malpighian follicles is not derived from the trabecular system, but is an outgrowth from the elastic tissue in the arterial wall (Fig. X).

Vascular System.—The branches of the splenic artery enter the spleen at the hilum and travel, for a space, in the trabeculae accompanied by the veins. In the trabeculae, the arteries retain their proper walls, while the veins lose theirs, the endothelium of the venous channels being based directly upon the trabecular tissue. As the arteries leave the trabeculae, they are accompanied by prolongations of the trabecular tissue



FIG. 10.—SPLENIC LOBULE. (Modified after Jordan.)

a, tunica serosa. *b*, tunica albuginea. *c*, trabeculae containing vein. *d*, vein. *ee*, branches of trabeculae inclosing "splenic unit." *f*, artery of lobule. *g*, lymphoid sheath of artery. *h*, malpighian body with germinal center. *k*, penicilli or precapillary arterioles. *m*, ellipsoid body. *p*, pulp cords separated by venous sinuses. *s*, reticulum arising from capsule.

which form a moderately thick fibro-elastic sheath about the main arteries. This sheath gradually comes to contain small-celled, large-nucleated elements and takes on the characteristics of lymphoid or adenoid tissue. The lymphoid sheath accompanies the small arteries and their branches and, from time to time, often at a point where the artery branches, develops thickenings which are the follicles or malpighian bodies. On leaving the last malpighian bodies, the sheath loses its lymphoid elements but remains rather thick for a short distance, after which the vessel suddenly terminates in a number of fine branches, the penicilli

or precapillary arterioles. These branches have a typical arterial wall but no sheath. Before going over into true capillaries, they develop another thickening of the wall, the so-called ellipsoid body. The ellipsoid body is well developed in the hog, but is rudimentary in man, consisting of a mere thickening of the wall inclosing some cells resembling plasma cells.

The course which is followed by the blood on its way from the arterial capillaries to the venous sinuses has been the subject of much discussion. Four theories have been proposed:

1. The arterial capillaries terminate abruptly with an open end in the pulp. The blood pours from the arterial capillaries into the splenic pulp and thence finds its way into the sinuses by means of spaces in the sinus walls. This theory thus supposes an intermediary circulation.

2. The arterial capillaries have open ends which discharge blood into the pulp, but, in addition, have a direct connection with the venous sinuses. The blood may, therefore, either go directly from the arteriole to the venous sinus or may first traverse the pulp. This theory proposes both an intermediary and a closed circulation.



FIG. II.—WALL OF VENOUS SINUS.

Diagram showing internal longitudinal fibers and external circular (sickle) cells and intermediate spaces.

3. There is only a closed circulation and the blood-cells can get into the pulp only by diapedesis.

4. A closed circulation exists, comprising a direct connection between the arterial capillaries and the venous sinuses. But the walls of the sinuses are full of openings and the blood readily escapes from the vessels into the splenic pulp and back again (Fig. XI).

The work of Mollier has lent strong support to the last of these theories. He describes the wall of the venous sinus as being composed of two elements. The inner layer is a longitudinal fibrous structure, the spleen fibers, rod cells or endothelial cells of other authors, with few nuclei and with spaces between the cells. The outer circular layer is made up of Henle's *Ringfasern*, which also have spaces between them. The cells of the outer layer have a large nucleus which projects somewhat and the cells have been called "sickle" cells. These layers are so arranged that with the dilatation of the sinuses, the openings become larger and the amount of blood found free in the spleen pulp becomes proportionately greater. Supported by this evidence and that of other recent investigators, the fourth of the above theories is the one most generally accepted.

The venous system begins with the junction of the smallest venous sinuses to form wider channels. By successive unions these channels become larger until they enter the trabeculae. In the trabeculae the venous endothelium is based directly upon the trabecular tissue and the veins do not acquire their proper walls until they reach the hilum. Here they leave the spleen and unite to form the splenic vein.

Malpighian Bodies.—The malpighian bodies or lymphoid follicles are recognizable, with the naked eye, in the cut surface of the spleen, as grayish, semitranslucent bodies, varying in size up to about 0.6 mm. in diameter. They are said to average about ten thousand in number in the adult spleen. As described above, they are thickenings of the lymphoid sheath of the arteries and are frequently placed at points where the arteries branch. They are thus always in close relation to the artery which is called the “central artery” of the follicle, although it is always situated eccentrically and there are frequently two of them. The malpighian body is an oval, spherical or cylindrical mass of cells, having

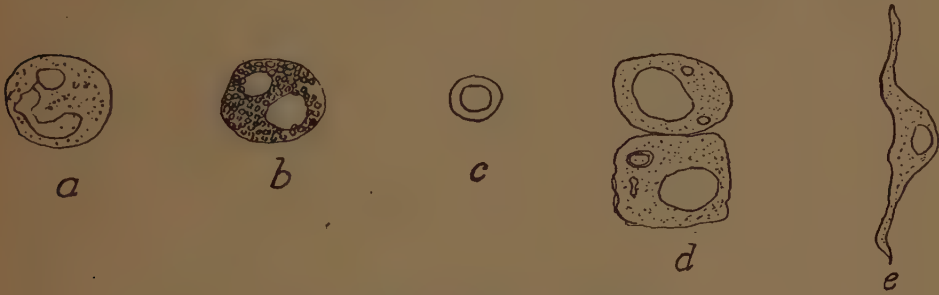


FIG. 12.—CELLS FOUND IN SPLEEN PULP.

a, polymorphonuclear neutrophil. *b*, eosinophil. *c*, lymphocyte. *d*, splenocytes or macrophages (upper one with vacuoles; lower, containing erythrocytes). *e*, sickle cell.

a structure similar to that of a lymph-node. In the center of the mass, in young individuals, the cells are larger and less closely packed, forming the “germinal center.” The nuclei of these cells are larger and have a less dense structure, and frequently mitotic changes are exhibited. It is believed that active proliferation of lymphocytes takes place in the germinal centers. With age, the germinal centers disappear and are few or entirely absent in middle life. The follicles also become smaller and less numerous and may disappear entirely in old age.

The periphery of the follicle is made up of a mantle of more densely packed small lymphocytes whose outer margin is rather sharply differentiated from the surrounding pulp tissue. According to Sobotta, the reticulum of the follicles is made up of two parts. There is a fine network of connective tissue fibers coming from the smallest branches of the trabecular system and, in addition, a delicate reticulum of elastic tissue fibrils which is derived from the elastic tissue layer of the arterial wall. Blood is supplied to the follicles by fine branches arising from the central artery (Fig. XII).

Splenic Pulp.—The pulp or proper tissue of the spleen is made up of venous sinuses, arterial capillaries, cellular elements and reticulum. The venous sinuses have a greater mass than all of the other components of the pulp combined, a construction which gives the spleen its characteristic soft consistence. The venous sinuses are arranged in the form of short anastomosing channels with fenestrated walls. The cellular elements are arranged in irregular cords, the pulp cords, and fill the spaces between the sinuses. The cells of the pulp cords are large mononuclear nongranular cells called splenocytes or macrophages, large and small lymphocytes, and, occasionally, megakaryocytes. In addition, the pulp tissue is saturated with blood that has escaped from the vessels and so contains all of the cells normally found in the blood, namely, red blood-cells, polymorphonuclear leukocytes, both neutrophilic and eosinophilic, large and small lymphocytes, large mononuclears or endotheliocytes, and an occasional mast-cell. There may also be found a few cells that are apparently myelocytes. These occur infrequently in man, but in some mammals may be so numerous as to make the spleen resemble the bone marrow (Sobotta). Nucleated red blood-cells are found only rarely in the normal spleen in man. The macrophages frequently contain fragments of erythrocytes believed to be in the process of destruction.

The reticulum is composed of connective tissue fibers derived from the smaller branches of the capsulotrabecular system and has no elastic tissue elements. The bundles of connective tissue fibers are covered with flat cells, each having a round or oval nucleus. In the young, these cells may have several nuclei. The name of reticulo-endothelial cellular system has been given to these fibers and their covering, and they are supposed to be of the same structure and function as the reticular system of the lymph-nodes. Stephan believes that these cells have an important function in connection with the proper coagulation of the blood (see section on physiology) and they are the cells which are believed to be chiefly affected in Gaucher's disease. Whether they are truly endothelial cells is not known. Some authors have seen in the fibers with their coverings, a special kind of fiber which they have called *Gitterfasern*.

Lymphatics.—The lymphatics of the spleen consist of a few channels which are found in the capsule and the trabeculae. There is reason to believe that the lymphoid tissue sheaths, which surround the arteries and in which develop the malpighian bodies are analogous to the perivascular lymph spaces. But these sheaths are apparently not true channels and cannot properly be classed as lymphatics. The finer structure of the splenic lymph-nodes has been described by Ciazio.

Nerves.—The nerves are nonmedullated fibers derived from the solar plexus of the sympathetic system. They supply the smooth muscle fibers in the capsulotrabecular system and in the walls of the arteries. Piersol says that some of the fibers in the pulp are presumably sensory.

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CHAPTER III

PHYSIOLOGY AND PATHOLOGY OF THE SPLEEN

PHYSIOLOGY

In spite of extensive investigation, little is actually known about the functions of the spleen. Many of the conclusions which have been published are still subjects of active controversy and it is only in minor details that physiologists and pathologists are in full accord as to its action. The problem has been attacked from several directions. Animals and man have been observed after splenectomy, both when the spleen was histologically normal and when it showed evidence of disease. Attempts have been made to determine its influence in various diseases by excising it and also by exposing it to the Roentgen ray. Fresh and dried whole spleen and extracts of the gland have been administered in various ways, both with the organ *in situ* and after its removal, in the effort to detect recognizable changes in body activity or, in the absence of the spleen, to discover evidence of a compensation for the loss of its activity. Other experimental investigations have been carried on, but results have been meager.

The microscopic anatomy of the spleen, while apparently relatively simple, is not fully understood. The organ has been regarded as an enormous lymphatic ganglion reacting in a general way to stimuli in much the same manner as all lymphatic tissue. But exceptions to this rule are sufficiently frequent to make them noticeable. Although the individual cells in the pulp and in the malpighian bodies are similar in appearance, there is evidence which suggests that they are components of different kinds of tissue. Manely and Marine made autotransplantations into the abdominal wall and found that they "took" well. After the transplantations were firmly established, they had the appearance of congested normal spleen. The malpighian bodies and the vessels had regenerated, and this fact led them to conclude that "either the vessels must be specific, which does not seem probable, or the lymphoidlike cells are specific in that they control and determine the blood-vessel arrangement."

It will facilitate the consideration of the subject if the functions of the spleen, whether established or hypothetical, are grouped under the following headings:

Internal Secretion.—Malpighi was the first to assert that the spleen produces an internal secretion, and this assertion has often been repeated,

but, up to the present time, no product of its activity has been satisfactorily demonstrated (Burton-Opitz). Downs and Eddy have obtained results which lead them to support Danilewsky's theory that this organ produces a substance in the nature of a hormone which stimulates the activity of the bone marrow. They administered protein-free extracts of the spleen to animals and observed a primary decrease in the number of red cells in the circulating blood. This decrease lasted for only two or three hours and was followed by a definite and more persistent increase, not only in the whole number of red cells, but also in the proportion of reticulated (young) erythrocytes. In rabbits, nucleated red cells appeared in the circulation and the resistance to hemolysis of the circulating red cells extended over a wider range than normally. In one of Pearce's experiments, a splenectomized dog which was dying from anemia was apparently saved by the administration of a splenic extract. Furthermore, Pearce found that blood regeneration proceeded more slowly in splenectomized than in normal dogs. But Moynihan points out that this latter effect may be due merely to the deprivation of the liver of the "effete" iron usually liberated by the spleen, combined in the liver and then furnished to the bone marrow. In addition, the feeding of spleen substance or splenic extracts, when attempted as a therapeutic measure, has produced no effects in the majority of instances. The results claimed by Harrower and Carpenter need confirmation before they may be accepted.

Leukocyte Formation.—These cells are formed in the follicles, most rapidly in infancy and young adult life when the "germinal centers" are most prominent and the percentage of lymphocytosis in the circulating blood is highest. Later in life the formation of these cells is less active. Their extension into the circulation is brought about, at least in part, by the contractions of the spleen. It is said that when the spleen is hypertrophied in lymphatic leukemia and its contraction is brought about by the application of an electric current, large numbers of lymphocytes are injected into the blood stream. After the injection of epinephrin, a lymphocytosis appears unless the spleen is severely pathologic.

Under ordinary circumstances, cells of the myeloid series, that is, myelocytes and polynuclears, are not produced in the spleen in man. But in myelogenic leukemia and in some forms of anemia, there are found in this organ foci of granular cells, some of which can be identified as myelocytes. These cells are apparently proliferating in the spleen, not merely deposited there by the blood stream, and are possibly furnished to the general circulation. This condition is called myeloid metaplasia or myeloidization. It is thought to be brought about by the transformation of cells in the spleen pulp into the parent cells of the myelocytes. It can be brought about artificially by the transplantation of bone marrow into the spleen, and Matsuoka is of the opinion that the myeloid deposits thus resulting are autochthonous in origin. The significance of myeloid metaplasia is not understood.

Erythrocyte Formation.—The question as to the part played by the spleen in the formation of erythrocytes is still disputed. The spleen is admittedly one of the chief hematopoietic centers in embryonic life, but most authorities believe that this activity ceases either at birth or shortly thereafter. At least this is generally accepted as being true in the human species. In certain of the anemias, there is a reversion to the embryonic type of blood formation, and the spleen again produces red cells. In lower animals the subject is very confused. The spleen exists in nearly all vertebrates, but is absent in certain fishes, such as the branchiostoma and myxine, although the blood of the latter contains numerous circular red cells. A very rudimentary spleen is found in the lamprey eel, the blood of which carries more round red cells than that of most other fishes.

In some animals, Morris found that the number of red cells in the blood of the splenic vein was greater than that in the artery and states that the cells were larger, more perfect, and seemed richer in hemoglobin. Krumbhaar and Musser do not accept this and are of the opinion that the slight difference found in the cell counts in the blood taken from these two vessels is probably due to technical errors in the methods used. Frey states that the red cells are fewer in the splenic vein than in the splenic artery. The possibility that the influence of the spleen upon red cell formation may be exerted indirectly by means of a hormone which acts upon the bone marrow, has been mentioned in a preceding paragraph. This possibility has not been demonstrated to be a fact and it must be concluded that, while the spleen exerts a certain influence upon erythrocyte formation, it is not directly concerned in this function in man in health and after birth.

Erythrocyte Destruction.—It has long been believed that the worn-out red cells are destroyed in the spleen. In 1848, B  clard obtained evidence which led him to this conclusion. Bieling and Isaac are of the opinion that, in the process of hemolysis which follows the injection of hemolytic immune serum, the amboceptor is bound in the circulation and that humoral, not intracellular, lysis occurs in the spleen. It was at first thought that the hemoglobin released by erythrocyte destruction in the spleen was carried to the liver and there made over into bilirubin. Of late years this belief has been somewhat modified and, at the present time, the theory most in favor holds that effete red cells undergo fragmentation in the circulation. The fragmented cells are removed from the circulation in the spleen where they undergo phagocytosis and possibly further fragmentation but where destruction is probably not completed. It is believed that the final steps in the process take place in the liver.

Banti and Furno claim to have found free hemoglobin in the blood of the splenic vein, but later investigators have not been able to confirm their findings. It has been suggested that possibly the hemoglobin is liberated in such form that it is not recognizable as such, but this is

hypothetical. On the other hand, it may be possible that the hemoglobin which is set free is converted to bilirubin in the spleen. This accords with Whipple's ideas, and Ernst and Szappanyos found that, if a solution of hemoglobin were supplied to a perfused "surviving" spleen, bilirubin was produced in fairly large quantities. Certainly, removal of the spleen does not result in a diminution of the output of bile (Burton-Opitz), and Warthin states that after splenectomy, hemolysis by the hemolymph-nodes may exceed that originally accomplished by the spleen. If it be accepted that the spleen is the principal site for the destruction of erythrocytes, it must be admitted that this function is promptly taken over by other organs when the spleen is removed.

Phagocytosis of the erythrocytes has been frequently demonstrated in the spleen and this is the organ where "hemolysis by macrophagia" is characteristically found. Red cells in various stages of fragmentation are found in the large lymphocytes and the splenocytes in the spleen pulp, to some extent in health, and, to a greater extent, in some forms of anemia. Steudemann demonstrated that phagocytosis of the red cells was never exhibited by the cells of the malpighian follicles, but occurred chiefly in the sinus endothelium. He considered it a peculiar function of the sinus endothelium as well as of the free macrophages.

The relation of the iron content of the spleen to the phagocytosis of red cells is obscure. Oppenheimer believes that the increase in iron content, which takes place in the spleen in the presence of increased hemolysis, is due directly to increased erythrolytic activity on the part of that organ. But the experiments of Addison suggest the possibility of another mechanism. Pigeon erythrocytes are hemolyzed by the rabbit. Addison injected pigeon's red cells into rabbits and found that bone marrow cells were liberated. These bone marrow cells were phagocytosed by the splenocytes when they reached the spleen and, at the same time, the iron content of the spleen was increased. This would indicate that the bone marrow may play some part in the process of erythrocyte destruction. Pearce, Krumbhaar and Frazier are of the opinion that the bone marrow takes over the function of the destruction of red cells after the removal of the spleen, and their evidence is, therefore, in a sense confirmatory of Addison's results.

The majority of the attempts to demonstrate hemolytic substances in extracts of splenic tissue have been unsuccessful (Robertson and Krumbhaar and Musser). Downs and Eddy injected protein-free extracts of spleen into rabbits and discovered a diminution in the number of red cells in the circulating blood which continued for about two or three hours. This fall was followed by a rise which they attributed to the action of a hormone upon the bone marrow, as mentioned in a preceding paragraph. But they believe the preliminary fall is due to a hemolytic action of the splenic extract. They found, when this extract was added to the diluting fluid during red cell counts, that the number of cells was less than when salt solution was used. Furthermore, the

greater the proportion of the extract, the greater was the reduction in the count. They contend that the failure of other investigators to demonstrate hemolytic substances in splenic extracts is due, at least in part, to the fact that they used washed red cells and thus eliminated the more fragile cells at the outset.

Strisower and Goldschmidt obtained results which seem to show that the osmotic resistance to hypotonic salt solution of erythrocytes from the splenic vein is less than that of red cells found in other vessels in the body. They were unable to demonstrate free hemoglobin in blood from the splenic vein, but did show the presence of slight hemolysis when the "surviving spleen" was irrigated with normal blood. This hemolysis was increased in amount after the animal had been poisoned with toluendiamin, a substance that injures the red cells and appears to increase the hemolytic powers of the spleen.

It may be concluded that the spleen plays an important part in the destruction of effete erythrocytes. It is not indispensable to the performance of this function, for red cell destruction proceeds as actively after splenectomy as in the normal individual. This function is, in part, brought about by phagocytosis, but the exact manner in which the disintegration of the cells is completed is not known. Although free hemoglobin has not been acceptably demonstrated in the splenic vein, it is possible that extracts of the spleen have some hemolytic power. It seems probable that the red cells are fragmented in the circulation, phagocytosed in the spleen and then sent to the liver for hemolysis, or that hemoglobin is extracted from the red cells in the spleen and changed into bilirubin or some other substance that has not yet been recognized. The material then goes to the liver for final disposition.

Purin Formation.—It is generally stated that the spleen plays an active part in purin metabolism and that the enzymes which form uric acid are more numerous in the spleen than in any other part of the body. Halliburton classifies them as nucleases and divides them into nucleinases, nucleotidases, nucleosidases, deamidases and oxydases.

Contractility.—The spleen has a spongy structure and the capsule and principal trabeculae contain smooth muscle tissue. It is supplied with vasomotor nerves, which lie in the plexus gastrolialis placed about the artery of the same name. Section of the splenic nerves results in a dilatation of the spleen, and stimulation of the peripheral cut ends produces a contraction. Stimulation of either splanchnic nerve results in a contraction of the spleen. By virtue of this neuromuscular apparatus, the spleen contracts rhythmically at a rate of about one per minute. This periodic contraction serves to renew the blood in the venous sinuses of the pulp and to aid the circulation within the organ. It probably also helps to force the newly formed lymphocytes into the circulation.

In addition to the regular contraction mentioned above and superimposed upon it, the spleen exhibits a distention during digestion. This

distention or dilatation is most marked at about the time that gastric digestion is finished. It has been suggested that, by this dilatation, the spleen serves as a blood reservoir for the portal system and thus regulates the degree of congestion in the liver and stomach. Moffitt thinks that the occurrence of gastric hemorrhage after splenectomy may be readily explained by attributing it to the removal of this regulatory influence upon gastric hyperemia.

The Spleen in Infection.—The spleen is frequently enlarged during the course of infectious diseases and it has long been surmised that this enlargement is an indication of the importance of the spleen in the defense of the body against infection. The structure of the organ resembles that of the lymph-nodes and, like them, it acts as a filter to remove small particles from the blood. It is probable, however, that its importance as a filter has been exaggerated, for Drinker and his associates have found that when minute particles of manganese dioxid are injected into the blood stream in animals, only a relatively small amount is found lodged in the spleen. By far the largest amount is found in the lungs and the liver. It is possible that bacteria may behave differently from inert particles because of chemotactic influences that may be exerted between the bacteria and the phagocytic cells. Ozaki believes that the accumulation of bacteria in the spleen is due largely to the activity of the spleen cells, not to filtration. It is true that phagocytosis of bacteria takes place in the spleen, but it is difficult to estimate the importance of this element in the body defenses. Under some conditions the efficiency of this phagocytic action is slight, for the spleen may swarm with infecting organisms, as in malaria, or may contain foci of infection, as in syphilis, that are so intrenched as to be affected relatively little by therapeutic measures.

The relation of the spleen to resistance and immunity has been thoroughly discussed by Morris and Bullock. These authors have reviewed the development of the subject since the time when Pfeiffer and Marx showed that immune bodies in cholera are present in the spleen and bone marrow in greater quantities than elsewhere in the body. Morris and Bullock used rats in their experiments and removed the spleen from one set. A series of control animals was subjected to the removal of one testicle so that disturbances resulting from operation might be the same in both series of animals. Their ultimate findings indicate that rats which have been splenectomized are more susceptible to infection with the bacillus of rat plague than are those from which one testicle has been removed. Removal of the spleen did not interfere with the development of immunity when the operation was performed before the introduction of antigen, but when antigen was introduced before splenectomy, antibodies were not formed.

Pryzgo has shown that agglutinins and specific precipitins can be formed by spleen tissue when it is grown in artificial cultures in the presence of horse serum. Wells claims that amboceptors are formed in

the spleen, since during the process of immunization they can be demonstrated in the spleen and hematopoietic organs before they can be recognized in the circulating blood. The formation of hemolysins in rabbits is unfavorably influenced by splenectomy.

Comelli found that splenectomy in a rabbit caused a lowering of the body temperature if the animal had been injected with pneumococci. He found pneumococci in the spleen within two hours after introducing them subcutaneously.

Exposure to the Roentgen ray and to radium produces a depression in the activity of the bone marrow and of all lymphoid tissue including the spleen. Hektoen and Curtis found that when such an exposure was made at or about the same time that an antigen was introduced into the body, it greatly interfered with the production of antibodies, as measured by their concentration in the serum. These authors were able to show that removal of the spleen diminished antibody formation, but concluded that this organ is not the only place in the body where antibodies are produced.

The question of immunity to tuberculosis is rather more confused than it is in regard to the acute infections. Morton exposed guinea pigs to the Roentgen ray, giving them one massive dose either immediately before or after they had been inoculated with urine containing tubercle bacilli. He found that animals so exposed developed tuberculosis more rapidly than his control animals and concluded that exposure to the X-ray diminished their resistance to this organism. Weinberg repeated and extended these experiments and was unable to detect any appreciable difference between the reactions of the exposed and of the control animals. On the other hand, Lewis and Margot found that the removal of the spleen from albino mice resulted in a well-marked though transient *increase* in the resistance of these animals to infection with the tubercle bacillus.

In certain chronic infections, especially syphilis and malaria, the infecting organisms may be found in the spleen in tremendous numbers, and Chavannaz and Guyot call it a veritable incubator for these organisms. Whether plasmodia and spirochetes are destroyed in the spleen is not known. It has been noted in a few instances that the removal of a large spleen in syphilis has been followed by an amelioration of the symptoms and a more favorable reaction on the part of the body to treatment (Coupland, Giffin). There is evidence at hand to show that benefit results from the removal of the nest of organisms which, for some reason, are beyond the reach of treatment.

On the basis of the available experimental results, it is justifiable to say that the spleen appears to play an important part in the development of the body's resistance to acute infections. But it is not essential, for, in the absence of the spleen, its functions are quite rapidly assumed by other organs. Antibody formation takes place in other portions of the body. In so far as the more chronic infections are concerned, there

are not at hand sufficient data to permit the arrival at definite conclusions. All of the experimental work has been done on animals and it has not been shown that a man who has lost his spleen is more or less susceptible to infection on that account. Nevertheless, the possibility that this function is an important one must always be borne in mind when the question of splenectomy arises.

The Spleen and Malignant Tumors.—It has long been recognized that it is unusual to find metastases of malignant neoplasms in the spleen. This fact is so striking that Segré felt that splenectomy might diminish the normal resistance to malignant growths. Blach and Weltmann state that when splenic tissue is mixed with rat sarcoma before injection into the animal there is evident a marked inhibitory influence upon the growth of the tumor tissue. But splenectomized mice are not more susceptible to tumor transplantations than are the normal animals, and tumor grafts will grow in the spleen itself. Graf injected tumor emulsions into various organs and obtained a higher percentage of "takes" in the spleen than in the liver, testicle, kidney or subcutaneous tissue.

This freedom of the spleen from metastases is relative. Kettle reports finding 8 splenic metastases in 240 autopsies upon cases of carcinoma. He has reviewed the literature of the subject. He mentions Taylor, who found 7 true metastases in the spleen in 677 cases of carcinoma and sarcoma; Paget, who found 17 in 735 cases of carcinoma of the breast; and Handley, who reported but 1 splenic metastasis in 422 cases. A summary of these four reports gives 33 cases in which metastases developed in the spleen in a total of 2,074 patients with malignant disease, an incidence of 1.5 per cent. Kettle emphasizes the fact that a diffuse malignant infiltration of the spleen may not be recognizable by the naked eye and that such instances may escape detection unless microscopic examination is made.

The reason for these findings has been attributed to three causes: the absence of afferent lymphatics; the sharp branching of the splenic artery from the celiac axis; and the characteristic rhythmic contractions of the spleen. Woglom thinks that these contractions do not permit metastases to find lodgment in the organ for a sufficiently long period to permit of their location and growth. This view is supported by Graf's observations. He found that it was possible to inject a tumor emulsion into the spleen and to get growths which developed only in the liver. Von Hansemann opposes this view and claims that splenic metastases are more frequent than is generally supposed. He says that he has often seen microscopic collections of tumor cells in this organ, but he does not describe them as actually growing metastases, and it is quite possible that what he saw were cells which were in the course of passing through the spleen and destined ultimately for the liver. If this is true, his findings may be taken as lending support to the deductions of Woglom, Graf and others. Deelman supports von Hansemann's claim that splenic metastasis are more frequent than is usually recog-

nized and says that they follow the involvement of the lung in the tumor process. Sappington in a recent review of the subject, with report of a case, supports Deelman's views. Kubik states that carcinoma metastasizes in the spleen only if the tumor penetrates a blood-vessel.

It may, therefore, be said that while the spleen is not likely to be the site of election for the location of metastases from malignant tumors, this is probably not due to any inherent resistance on the part of the spleen to the growth of tumor cells, but rather to the characteristic rhythmic contractions of that organ.

Coagulation of the Blood.—Stephan claims that exposure of the spleen to the Roentgen ray results in a marked shortening of the coagulation time and an increase in the "coagulating ferment" of the blood serum. The platelet count is not modified. The coagulation time was reduced to one fourth in normal subjects. The maximum effect was reached between two and four hours after the exposure to the X-ray and then gradually subsided, reaching normal by the eighth hour. He attributes this effect to a stimulation of the splenic tissue other than the lymph follicles, the reticulo-endothelial cellular system. He believes that "stimulating the function of the spleen by Roentgen radiant energy must be regarded, theoretically, as a true physiologic method of arresting venous and parenchymatous hemorrhage." He was able to check the hemorrhage in a case of purpura by this means and considers the method important. His observations have been confirmed by Vogt, Jurasz, Tichy and Hütten, though Hütten was unable to discover any effect upon hemorrhage at operation as a result of this procedure. Tichy obtained a similar effect by irradiation of the liver. Nonnenbruch and Szyszka claim that a similar but more brief effect may be obtained by diathermy. Opposed to these findings, to some extent, is the work of Henn who found that after the removal of the spleen in dogs there is a shortening of the coagulation time. Ohara found no influence on the coagulation time of the blood in rabbits after the injection of spleen juice.

Miscellaneous.—In addition to the above more or less well-defined functions, there are probably many others which have not yet been recognized. Some of them have been hinted at in various observations to be found recorded in the literature, but it is often difficult to correlate them with what we now accept as fact. Others have been described but have not yet found sufficient corroboration to force their general acceptance. One idea appears in most of the discussions, namely, that when the spleen is removed, its functions appear to be taken over readily by other organs, for the absence of the spleen is not in any way incompatible with what seems to be perfect health in man.

Von Hanseemann found that splenectomized animals were much more sensitive to cold than normal animals, and that, when exposed to cold, they were more apt to develop a hemorrhagic nephritis. He observed further that if a hedgehog were splenectomized in the spring,

it was as unusually susceptible to cold as were other splenectomized animals, but if the operation were performed in the fall when the animal was prepared for its winter hibernation, the removal of the spleen was apparently without effect in this respect. Mann and Drips found that the spleen in hibernating animals showed intense congestion and that as the hibernating period neared its end the congestion gradually diminished.

Morse found in the spleen certain enzymes which he called proteoclastic tissue enzymes and which were capable of hydrolyzing peptone and fibrin. He observed their most rapid action in acid solutions having a pH value of 5.68. But Wells states that it also contains an enzyme which is active in alkaline solution. He explains that the spleen and the blood contain antibodies which check the action of the enzyme in alkaline solutions, whereas acids destroy this antibody and, for that reason, the enzyme acting in acid media appears more prominently. Hedin found two proteases and an erepsin in the spleen.

The spleen is apparently concerned with iron metabolism, though in what way is not known. Oppenheimer calls it a storage depot for iron and believes that its reserve supply is called upon only when the iron content of the food is low. The iron excretion has been found to be increased in splenectomized animals (Pearce, Krumbhaar and Frazier). It may be that this storage ability is connected in some way with the preparation of hemoglobin or some of its constituents.

Oppenheimer states that some of the functions of the spleen are opposed to those of the thyroid gland. He says that under certain conditions thyroidectomized animals exhibit symptoms of oxygen deficiency to a slight degree or very slowly or even not at all. Splenectomized animals under the same conditions show symptoms unusually quickly. Animals from which both the spleen and thyroid have been removed behave like normal animals in the symptoms which they present and in the period within which these symptoms appear. But Moynihan refers to the work of several investigators whose results are contradictory. About all that can be said is that some correlation of the activities of these two organs is suggested by the experiments that have been performed. Oppenheimer also makes the statement that the spleen regulates the cholesterin content of the blood, but no reliable figures are available on the subject, except that the blood cholesterin is increased after splenectomy.

Injection of an extract of spleen powerfully stimulates the muscular activity of the intestine and, under the name of "hormonal," such an extract was exploited commercially several years ago as a means of treating postoperative ileus, constipation, etc. It is said to produce its effect by its action upon the vagus, and it is thought that a part of the function of the spleen is to preserve the normal tone of the gastric and intestinal musculature (Stern and Rothlin). Its therapeutic use was followed, in a number of instances, by unpleasant effects upon the vaso-

motor system—collapse, etc.—and the preparation is now rarely used.

It has long been supposed that the spleen exerted some influence upon digestion and many contradictory statements have appeared on this subject. The matter has been investigated recently by Inlow and by Mollow, who have shown quite definitely that it is impossible to demonstrate any influence exerted by the spleen upon gastric or pancreatic digestion, gastric or duodenal peristalsis or the secretion of bile.

Effects of Splenectomy.—One manner of studying the functions of an organ is to determine the effects of its removal from healthy animals. This has been done to a large extent in the study of the spleen. Splenectomy is not a fatal operation and has been performed upon many individuals who have remained in apparently excellent health for years after the operation. Henn has confirmed previous assertions that splenectomy in the young has a negligible effect upon growth. He employed rats and rabbits in his experiments. A number of splenectomized women have passed through normal pregnancies. In some instances, splenectomy during pregnancy has had no effect upon either the mother or the child. In other cases, miscarriage or stillbirth has occurred in splenectomized women. Our patient, who was splenectomized for Gaucher's disease, passed through pregnancy and delivery without ill effect.

Pearce and his collaborators have investigated the subject quite extensively and frequent reference will be made to their results. It must be remembered that the present physiological consideration will be confined to the effects of the removal of the normal spleen as determined experimentally in animals or when performed for injury to that organ in man. The effect of the removal of a diseased spleen may be quite different; this will be considered individually as each pathological condition is discussed.

After splenectomy in normal animals, there develops, either immediately or after a short delay, an anemia, secondary in type, which disappears in the course of from two and one half to three months. The administration of iron does not seem to hasten recovery from this anemia. Wolferth is of the opinion that this anemia is probably of hemolytic nature, but he does not offer very convincing evidence to support his opinion. When splenectomy is performed for traumatic rupture of the organ, the anemia does not seem to be more severe than would be expected from the loss of blood attending the accident and the operation. This has been the case in the several instances which have come to our attention. There also appears, following the operation, a leukocytosis and a polynucleosis and often a moderate grade of eosinophilia. After the subsidence of the leukocytosis, there may appear a lymphocytosis which may persist for a year or more, but this is not the usual effect. Abnormal cells such as normoblasts and myelocytes are rarely found in the blood stream after this operation. In one case Morris found after splenectomy, an increase in the number of red cells which

contained fine, round basophilic particles which stained with all the nuclear dyes. He interpreted them as being nuclear particles. Gilbert found Howell-Jolly bodies in the erythrocytes after splenectomy and says that they have been found for as long as seven years after operation. He suggests that the spleen may normally effect the disappearance of the nuclear material from the red cells.

In Hall's case of splenectomy for rupture, the leukocyte count rose to nearly 20,000 during the first sixteen days after the operation and remained rather higher than normal during a period of about three months. During the entire period, the polynuclear percentage varied between 37 and 73. There was a slight but persistent increase in the percentage of the large mononuclears and transitional cells, the so-called endothelial cells. These blood changes are, however, but temporary. In three patients subjected to splenectomy for traumatic rupture, whom we have seen for varying periods after operation, the blood count was normal by the end of a nine-month interval. The moderate lymphocytosis found in one case was no more than one would expect in a child of its age. Kreuter emphasizes the fact that permanent changes in the blood of healthy animals after splenectomy have not been reported.

Pearce demonstrated that there is an increase in the resistance of the red cells to hemolysis after removal of the spleen. This is apparent whether the hemolytic agent used is hypotonic salt solution, saponin, toluendiamin or hemolytic immune serum. This increased resistance is probably due to some change which takes place in the red cells themselves. When such hemolytic agents are administered to splenectomized animals, there becomes evident a lessened tendency to produce jaundice as compared with the effect of these substances upon normal animals. Nevertheless, the animals so treated develop an anemia which is more severe and more lasting than that produced by these agents in normal animals. This paradox is difficult to understand. Pearce believes that the increased resistance of the red cells and the decreased tendency to jaundice are intimately associated with the anemia of splenectomy, but that the anemia itself depends upon some unknown factor. Moynihan is inclined to attribute it to the loss of the normal splenic ability to furnish *effete* iron to the liver. The latter organ being deprived of adequate supply fails to manufacture for the bone marrow sufficient complexly combined iron to permit of rapid hemoglobin formation. This explanation is purely hypothetical.

On the basis of numerous experiments, Pearce explains the lessened tendency to jaundice as being due to a diminution in the concentration of the products of erythrocyte disintegration as they reach the liver. Normally this process takes place chiefly in the spleen and the products reach the liver in concentrated form. A relatively slight increase in this concentration is quickly appreciated by the liver, and jaundice results. After the removal of the spleen, red cell fragmentation is carried on chiefly in the bone marrow. This tissue is located at such distance

from the liver that the products reach that organ in a relatively dilute form and it takes a much greater increase in hemolysis to raise the concentration sufficiently to produce jaundice. According to this theory, jaundice becomes an index to the site of red cell destruction rather than of the degree of such destruction.

After removal of the spleen, there is an increase in the excretion of iron (Pearce, Asher, Grossenbacher). Pearce is inclined to attribute this directly to the anemia and thus only indirectly to the absence of the spleen. Oppenheimer, however, ascribes it to the absence of the splenic function of iron storage.

King found a decreased output of total fat in the feces and an increase in the fat and cholesterin in the blood. This increase in the amount of blood cholesterin is thought to aid the resistance of the red cells to hemolytic agents. The elimination of fatty acids is said to be increased.

There is a diminished output of uric acid and urobilin in the urine and feces (Goldschmidt, Pepper and Pearce). The diminution of uric acid is attributed to the removal of the splenic influence in uric acid formation. The change in urobilin output is possibly related to changes in the process of red cell destruction which follow removal of the spleen, or it may be associated with the increase in blood cholesterin and the increased resistance of the erythrocytes. The urinary chlorids are decreased and the calcium, though unchanged in the urine, is definitely increased in the feces. The nitrogen in the urine is said to be increased.

Following splenectomy, the bone marrow usually changes from the normal yellow fatty type to a red cellular hyperplastic condition. This change is generally complete after from six to twenty months, but exceptions to the rule have been observed. This hyperplasia is not compensatory to the anemia. The red marrow is rich in iron and it is possible that in the absence of the spleen the marrow may store iron.

King, Bernheim and Jones found an increased ability of the splenectomized animal to retain transfused blood. It is probable that this change is associated with the splenic ability to destroy effete erythrocytes and that in the absence of the spleen this function is not carried on so intensively by the marrow.

Towles has shown that there is no difference between normal and splenectomized mice in respect to the lethal dose of arsenic for these animals.

Richet believes that, after splenectomy, it is necessary for animals to receive a larger supply of food than normally in order to maintain their weight. Hitzrot was unable to substantiate this claim in his observations upon healthy men who had been splenectomized. Smith and Ascham found no evidence of increased appetite nor of variation from the normal growth rate in splenectomized rats.

The thyroid enlarges sometimes after removal of the spleen. The significance of this change is not known, but the observation supports

the claims of those who believe that the two organs are in some way related in their activities. Removal of the spleen produced no specific changes in the thymus but seemed to make the animal less able to withstand the stress of life (Mann).

Following splenectomy, any splenic tissue remaining in the body undergoes rapid and extensive hypertrophy. Eccles and Freer report a remarkable instance in which an abdominal operation, performed eight years after a splenectomy for rupture in malaria, revealed the presence of a spleen which was normal in size and appearance. Faltin, six years after, and Küllner, five years after splenectomy, found numerous small nodules of splenic tissue in the abdomens of their patients. Some think these may have been due to the accidental implantation of minute fragments of splenic tissue at the time of operation. Faltin explains it, rather more plausibly, as a supplementary growth of latent hemolymph-nodes. Microscopic areas of lymphoid tissue have been described in numerous organs and places in the body, and it is possible that some of them represent potential splenic tissue.

After removal of the spleen, there is a compensatory hypertrophy of lymphoid tissue throughout the body. There is generally an increase in the number of endothelial cells in the lymph-nodes and these cells may become phagocytic for erythrocytes if hemolytic immune serum is administered. Similar phagocytosis may be observed in the Kupffer cells of the liver which are also said to increase in number and to contain hemosiderin. This suggests that a compensatory function is developed in the liver and lymph-nodes. If so, it is developed rapidly and completely.

Summary.—The apparent functions of the spleen may be enumerated in their order of probability, as follows:

1. Promotion of splenic circulation by contractility.
2. Formation of lymphocytes.
3. Partial destruction of erythrocytes.
4. Filtration of the blood (bacteria and inert particles).
5. Production of immune substances.
6. Formation of purins.
7. Storage of iron.
8. Production of a hormone which maintains the tone of the muscles of the gastro-intestinal tract.
9. Production of a hormone which stimulates the production of red cells by the bone marrow.
10. Regulation of hyperemia in the liver and stomach.
11. Production of some substance which facilitates the coagulation of the blood.
12. Production of proteoclastic tissue enzymes.
13. Regulation of blood cholesterin.
14. Protection against the effects of cold.
15. Antagonism to the thyroid.

PATHOLOGY

From what has been said in the sections on physiology and histology, it can readily be understood that the pathology of the spleen is obscure in many respects. It is comparatively simple to record the changes that have been observed in various diseases, but a study of these records will show that the histologic picture is rarely pathognomonic. Gross says that a constant specific reaction to a stimulus or a uniform expression of a disease does not exist. There is no type of cell which is characteristic of the spleen unless it be the so-called "sickle" cells in the walls of the venous sinuses. In Gaucher's disease and tuberculosis, generally in Hodgkin's disease and the neoplasms, and often in myelogenous leukemia, the diagnosis can be made after examination of a section from the spleen. But apart from these, similar morphologic changes may be seen in several pathologic conditions, and one disease may show, at different times or in different individuals, variations in microscopic structure that bear little resemblance to one another. Furthermore, the age of the patient has a strong bearing upon the interpretation of the changes found. One need only mention the confusion existing in respect to the pathology of the spleen in cirrhosis of the liver, syphilis, splenic anemia and von Jaksch's disease to furnish examples of this lack of specific reaction.

Congestion, anemia, atrophy, hyperplasia, metaplasia and fibrosis are the principal changes found, and they may appear in various combinations and proportions in such a confusing manner that the pathologist is frequently quite unable to offer a diagnosis and must content himself with describing such deviations from the normal as he is able to recognize. Thus, in the realm of the diseases of the spleen, perhaps more than in other fields, he is forced to relegate morphology to a position of subsidiary importance and call to his aid all of the information obtainable upon investigation by clinical, bacteriological, immunological, serological and clinical pathological means, before he is able to arrive at a proper diagnosis.

We shall include in the present section a brief presentation of the pathology of the spleen as a whole. The description, at this point, of the various degenerations, inflammations and circulatory changes will, we believe, help to furnish the reader with a clearer conception of the entire subject and at the same time avoid the necessity for subsequent repetition. No description will be included here of those conditions which will receive detailed consideration later.

Postmortem Changes.—The spleen is extremely vascular and it should be appreciated that, as a result of the escape of blood which occurs at death or when the organ is removed or incised, its appearance and size may be greatly altered. Autolysis takes place in the spleen rather more rapidly than in many other organs and, in consequence, postmortem material is often not faithfully representative of the condi-

tions existing during life. Organs removed in the operating room must be fixed within a brief period if autolytic changes are to be avoided. With the death of the organ, the color becomes darker and the consistence softer. This diminution in consistence is less marked in old age, when atrophy has occurred, and in those conditions in which fibrosis is present. The malpighian bodies may lose their sharpness of outline. Microscopically, there is apt to be degeneration of the cellular elements so that they are less easily recognizable. Hemolysis may occur with consequent diffuse staining of the tissue with hemoglobin. Care must be exercised not to confuse the softening caused by postmortem changes with that seen in the so-called "acute splenic tumor," that is, the acute splenitis seen in infectious diseases.

Age Changes.—During intra-uterine life, the spleen contains foci of red cell formation. These have disappeared at birth. During early life the organ exhibits evidences of great activity. The lymphoid follicles are large and distinct and have large germinal centers. The pulp is cellular and loose in structure and the sinuses are large. At the time of puberty, changes have begun to occur. The germinal centers of the follicles disappear and the pulp becomes more condensed. A little later, connective tissue changes are found. Gross says that hyaline changes are seen in the blood-vessels in practically every spleen over thirty-six years of age. At about fifty years we are able to recognize definitely the tissue changes which characterize atrophy.

Atrophy.—Atrophy occurs in old age, cachexia, anemia and in some chronic diseases. It is marked by a shrinkage in the size of the organ which may weigh as little as 20 gm. It is grayish blue and may present small, pale, elevated nodules which are localized thickenings in the capsule. The capsule is wrinkled. On section, the consistence is firm and tough. The cut surface is bluish red or pink, the pulp appears dry and homogeneous and the trabeculae are prominent. Early in the process, the lymphoid follicles are diminished in size and number and later they disappear. On microscopic examination, the follicles are few and small and show no germinal centers, or they may be entirely absent. The capsule is thickened and shows round cell infiltration. The trabeculae are relatively and absolutely thickened and the vessel walls are thickened and show hyaline changes. The vessel sheaths and the pulp may contain amorphous brown pigment. The venous sinuses contain little blood and are compressed. The pulp is condensed but contains fewer cells than in the young spleen. It occupies a relatively large proportion of the organ because of the collapse of the sinuses.

Fatty Degeneration.—Fat may be found in the endothelial cells in diphtheria and scarlet fever and in the hyaline areas in the arterial walls in acute infections and in arteriosclerosis. Large mononuclear cells containing fatty or lipid granules are found in several conditions, notably diabetic leukemia.

Hyaline Degeneration.—Hyaline degeneration occurs in the follicles

as a thickening of the reticulum and in the walls of the arteries in acute infections and arteriosclerosis.

Amyloid Degeneration.—Amyloid degeneration appears in chronic infections, pyogenic, syphilitic and tuberculous, and in Hodgkin's disease. It is not really a degeneration but a true infiltration, the amyloid substance being found not in the cells but between the capillary endothelium and the adjacent cells. It is seen in two forms.

1. The "sago" spleen in which the amyloid material is deposited chiefly in and about the follicles. The organ is moderately enlarged, rarely weighing as much as 500 gm. It is pale red and hard. On section, the cut surface is pale red, studded with bright gray, translucent, shining, projecting nodules which resemble cooked sago grains. The appearance has been thought similar to that of red wine soup with sago. These nodules stain a mahogany color when treated with a solution of iodine. Microscopically, we find the amyloid substance deposited in the walls of the small arteries and the reticulum of the surrounding follicles, and, at times, also in the walls of the capillaries. The reticulum fibers have the appearance of swollen glassy cords. A narrow rim of lymphoid tissue often remains at the periphery of the follicles. Occasionally foreign-body giant cells are found at the margin of the mass of amyloid.

2. The "ham," "bacon" or "waxy" spleen, in which the amyloid material infiltrates the pulp or both the pulp and the follicles. The spleen is rather larger than in the sago form and is plump. The capsule is tense and often very thin. On section, the cut surface is the color of smoked ham or cooked bacon and has a smooth, homogeneous and glassy or waxy appearance. The follicles are small and atrophic or not recognizable with the naked eye. The trabeculae are readily seen. On microscopic examination, we find deposition of masses of amyloid material between the trabeculae, in the reticulum fibers, in the walls of the arteries, capillaries and venous sinuses and sometimes also in the follicles. Many of the vessels are occluded. The pulp cords are compressed and the follicles atrophic. It may be impossible to differentiate slight grades of these two types of amyloid infiltration without microscopic examination. The iodine test is of importance in establishing the diagnosis.

The amyloid spleen does not of itself cause symptoms, and rarely becomes large enough to produce mechanical disturbances. It is merely one of the evidences of an underlying disease and does not demand treatment.

Roentgen Ray Effect.—After the use of the X-ray or of benzol in leukemia, there has been observed a peculiar induration of the spleen (Schridde). The organ becomes smaller and is pigmented. There develops a connective tissue thickening of the capsule and the pulp is permeated with a fine fibrillar network. The pulp cells are diminished in number.

Pigment Deposition.—In carrying out its functions as one of the filters of the circulating blood and as an important center for red cell disintegration, the spleen becomes a depot where pigment and various foreign particles are collected. This condition is seen after experimental injections of India ink and similar substances and also in such diseases as malaria, in which pigment set free in the blood is, in part, removed from the circulation by the spleen. Carbon particles are occasionally found in the spleen in the condition known as secondary anthracosis. In those types of disease in which there is increase in the destruction of erythrocytes, whether it takes place in the blood as it does in malaria, or in the spleen as it is believed to do in hemolytic icterus, one of the effects is a marked increase in the pigment content of the spleen. The pigment may be hemosiderin, melanin or methemoglobin. The enlargement of the spleen which so often accompanies increased blood destruction is believed to be an expression of the erythrocyte-destroying activity of the organ and has been called "spodogenous splenomegaly."

The size of the spleen in cases of pigment depositions depends upon other lesions present rather than upon the pigment. The appearance of the organ is altered only when the amount of pigment present is large. In that case, the color may be brown or gray or yellow, depending upon the nature of the pigment. The pigment granules are found in the macrophages, the endothelial leukocytes and the splenocytes which are apt to be found collected in clumps around the arteries and trabeculae as if for the purpose of digesting the pigment.

In cases of jaundice, the whole spleen may be diffusely stained with bilirubin, or crystals of bilirubin may be found within the macrophages. Hematoidin crystals may be found in old organized hemorrhagic infarcts.

Circulatory Disturbances.—Because of its abundant blood supply and intimate connection with the general circulation, the spleen is readily affected by all of those conditions in which there is a change in the circulation of the body as a whole. In acute infections, there is added to the congestive effect the action of the toxins of the disease and often the result of the collection in the spleen of the bacteria which are producing the infection. It is believed that the tendency of bacteria to collect in the spleen is due, not solely to the filtering powers of the organ, but, largely, to the activity of the phagocytes within it. It is possible to recognize the conditions of active hyperemia, acute congestion, acute splenitis and suppurative splenitis, but these are actually only steps in a progressive change from one extreme to the other. Each step merges gradually into the next and it is difficult to differentiate between two conditions in border-line cases.

Anemia.—In simple anemia, the spleen is small, pale grayish red, and the capsule is wrinkled. On section, the consistence is flabby and rather tough. The cut surface is pale red and the follicles are not recognizable. Microscopically, the venous sinuses are collapsed and the pulp cells diminished.

Active Hyperemia.—This is the mildest degree of increase in the blood content of the spleen. It may be physiologic, for the spleen is engorged with blood at the height of digestion. It is a temporary condition and is characterized histologically only by a dilatation of the venous sinuses and an increase in the number of erythrocytes found in the pulp. When it occurs as the first stage of the reaction of the organ in acute infectious diseases, it may be considered pathological.

Acute Congestion.—The second step of the splenic reaction to infection is acute congestion. It is much more frequent in acute infection but apparently occurs in the more chronic types as well, for Villaret claims that a transient enlargement of the spleen is one of the earliest signs of tuberculosis and the large soft spleen of secondary syphilis is probably of the same nature. Acute congestion differs from active hyperemia only in degree. The difference is possibly due in part to the action of the toxins of the infection, but their effect is slight. The spleen is slightly enlarged, its color dark red and its capsule tense. On section, blood readily escapes from the cut surface, which is dark red; the consistence is soft; and the malpighian bodies are readily visible. Histologically, the venous sinuses are widely distended and the pulp is engorged with blood. Acute congestion is a temporary condition and soon regresses or passes on to acute splenitis.

Acute Splenitis.—Acute splenitis or septic spleen is the condition which was originally known as "acute splenic tumor." The double meaning which has been acquired by the word *tumor* has made its use undesirable in descriptive writing and we shall attempt to avoid it despite the fact that the strict meaning of the word makes it especially suitable in a discussion of the enlargements of the spleen. Acute splenitis occurs only in acute infections. It is particularly well marked in typhoid fever and the bacteremias. The organ is enlarged up to 600 or 700 gm. It is soft, sometimes almost fluid, and the capsule is thin and tense. This combination of swelling and soft consistence renders the spleen liable to rupture upon the application of but slight trauma. Exploratory puncture of the spleen is a dangerous procedure in the presence of this condition. Acute splenitis has been carefully studied by MacCallum and his associates, who have described two types, a red and a gray.

The red type is found characteristically in typhoid fever. It is larger than the gray type, Evans' cases averaging 387 gm. in weight. The spleen is dark red and the capsule thin and tense. As the organ is cut, the pulp bulges out and obscures the trabeculae. The consistence is extremely soft, like paint or even a soft jelly, and the pulp can readily be scraped away with the knife, leaving behind the trabeculae as projecting shreds. The follicles are but little changed and are visible when not obscured by the bulging pulp. In some instances they may be marked by a central, minute, opaque, yellowish spot. On microscopic examination, there is found an enormous increase in the number of red cells, both in the sinuses and in the pulp. There is a hyperplasia and

hyperactivity of the macrophages, which are seen to be filled with erythrocytes in various stages of fragmentation. The other cells of the pulp are decreased. In typhoid fever, there may be found central necrosis of the follicles similar to that seen in the lymph-nodes and Peyer's patches.

The gray type is more frequently encountered in streptococcus, staphylococcus and pneumococcus bacteremias, scarlet fever, diphtheria and other infections. The color is dark grayish red and the consistence, although soft, is firmer than that found in the red type. The spleen is slightly smaller than the red type. Evans' cases averaged 324 gm. On section, the pulp bulges to a less extent and the follicles and trabeculae are more readily visible. The pulp is drier and scrapes off less readily. On microscopic examination, there is found less congestion and more hyperplasia. The venous sinuses are more or less compressed and the pulp cells are numerous. There is comparatively little blood in the sinuses and the pulp. Phagocytosis is not marked, though occasional active macrophages are found. In scarlet fever, there may be evident phagocytosis of blood-platelets. In some infections, especially in diphtheria, there may be found a mass of large pale phagocytic cells in the center of the malpighian body. The nuclei of these cells eventually become fragmented and the masses take on the appearance of focal necrosis.

It has been claimed that the red type is the early stage of acute splenitis and the gray type is the later or more advanced stage. This question remains undecided, but the studies in MacCallum's laboratory indicate that the two conditions tend to develop along lines depending upon the nature of the infecting agent, probably the nature of its toxin, rather than upon the stage of the process. In our experience, the gray type is found relatively infrequently no matter what the nature of the infection.

With the recovery of the patient from the infection, the acute splenitis subsides and disappears, leaving no recognizable traces. It is probable, however, that some permanent effect remains, for, after repeated attacks of certain infections, we find definite and permanent changes in the spleen. These changes are usually said to be due to recurrences of acute splenitis.

Except in so far as it may lead to rupture, acute splenitis does not demand treatment. Occasionally the process is long continued and unusually severe. Polynuclear neutrophils appear in the pulp cords and may become so numerous as to warrant the designation of acute suppurative splenitis.

Acute Suppurative Splenitis.—Acute suppurative splenitis occurs in two forms, both of which are rare. As a sequel to acute splenitis, there may develop a progressive infiltration of the spleen with polynuclear leukocytes, gradual softening of the organ and necrosis until the whole spleen becomes a mere bag of pus held together by a thin, tense capsule and

a few shreds of trabeculae. The second form results from numerous minute septic emboli, and the picture is one of multiple miliary abscesses rather than a large single abscess. Follicular abscesses develop rarely and usually undergo resolution spontaneously.

Hemorrhage.—Hemorrhages may be found in the spleen in infectious diseases. They appear as fine dark red points and are often difficult to differentiate from stasis. At other times, the hemorrhage may be large and has been called intraparenchymatous hemorrhage (Baird). Some of these are really subcapsular ruptures, while in others the hemorrhage begins in the interior of the organ. It is believed that the underlying lesion in this condition is a primary simple or hemorrhagic splenitis of unknown cause. When the hemorrhage is large, the capsule may rupture and allow the escape of blood into the peritoneal cavity with subsequent death of the patient. If the capsule remains intact, the spleen may be entirely disintegrated and transformed into a gelatinous mass of fibrin inclosed in a connective tissue wall. Intraparenchymatous hemorrhage is a rare condition.

Chronic Passive Congestion.—Chronic stasis or cyanotic induration of the spleen occurs when there is persistent obstruction to the outflow of blood from that organ. Two forms have been described: the central form in which the splenic congestion is part of a general stasis throughout the body; and the peripheral form in which the obstruction is located in the portal system. As a general rule, the portal stasis is of comparatively brief duration due to the early establishment of a collateral circulation, and the changes found are, therefore, less marked.

Whether pure stasis in itself can bring about an increase in the amount of fibrous tissue in the spleen is a question that has been much debated. One difficulty in the solution is that absolutely pure and uncomplicated stasis is practically nonexistent. In general chronic passive congestion, the tissues of the body suffer from the effect of the toxic substances resulting from the reduction in oxidative processes, really an acidosis. In addition, there may be specific effects of the underlying cause of the congestion. In local portal obstruction, the condition is practically always complicated by the underlying disease. The attempt has been made to differentiate between the findings in the spleen in the central and peripheral forms of stasis (Nishikawa) and, in fact, differences can at times be demonstrated. But they generally consist in a difference in the degree of pathologic change rather than in the nature of the lesions found. The macroscopic appearance is often more characteristic than the microscopic picture, due largely to the ease with which the blood escapes from the fragments of the spleen when they are cut away.

In chronic passive congestion, the spleen is only moderately enlarged, rarely weighing more than 400 gm. It is dark bluish red, rounded in contour, hard and confined within a moderately tense capsule. If the congestion has existed for a very long period, the spleen

may be small, wrinkled and atrophic. On section, the consistence is hard and resistant in spite of the increased blood content. It is apt to be somewhat softer in the peripheral than in the central form of stasis. The cut surface is dark red. The malpighian bodies are at first easily visible, but as the stasis persists they gradually become compressed and atrophic. The trabeculae may be slightly thickened. On microscopic examination, there is evident an early engorgement of the spleen with red cells. In extreme examples of this condition, the walls of the sinuses are recognized only with difficulty and the whole spleen pulp has the appearance of what has been called a "blood lake." There is a moderate thickening of the capsulotrabecular system and the walls of the venous sinuses. Nishikawa claims that, in the peripheral type of stasis, it is possible to recognize an extension of delicate elastic fiber threads into the pulp, an appearance not found in chronic congestion of central origin. The venous sinuses are irregularly dilated and distended with blood and their walls show an increase in elastic tissue content. The cells in the pulp cords are not increased and may be diminished. The reticulum fibers may have a hyaline appearance. The condition may be summarized as congestion associated with a mild grade of fibrosis.

In cirrhosis of the liver and in splenic anemia or Banti's disease, the spleen is enlarged and shows a chronic interstitial splenitis associated with a certain amount of hyperplasia and often with perisplenitis and sclerosis of the vessels. These conditions will be discussed at length in the sections devoted to these diseases.

Embolism.—The arteries of the spleen are terminal vessels so that embolism usually results in infarction. Emboli originate chiefly in the left heart and the result of their lodgment differs, depending upon whether they are simple or infectious.

Simple emboli may plug a vessel of any size. The resultant lesion is an anemic or a hemorrhagic infarct. These two varieties differ, in that, in the hemorrhagic form, there is a flooding of the infarcted tissue with blood through small collateral branches of the vessel. The early appearance is that of a dirty, pale red, roughly pyramidal portion of the organ, whose size depends upon that of the occluded vessel. Necrosis of the cells in this segment occurs and a consequent softening of the tissue. The cells of the follicles apparently possess more vitality than those of the pulp, for they are the last to die. At the periphery of the necrotic tissue, there is a hyperemic zone of varying width which shows a rich infiltration with leukocytes. Dehydration gradually occurs, followed by resolution or organization, with the formation of a pale yellow or, later, an almost pure white, hard segment of scar tissue. If the infarction was originally hemorrhagic in type, the final scar has a brownish tinge and shows hematoidin crystals. With subsequent contraction of the scar tissue, especially if the infarcts are multiple, there is more or less deformation of the spleen and depression of the scar. Lime salts may be deposited in infarcts during the healing process. When the splenic

artery is occluded, the entire organ may pass through these changes.

If the embolus is infectious, the necrotic tissue becomes an incubator for the development of bacteria and is surrounded by a suppurating zone. The infarct softens and becomes an abscess. Since this abscess is in contact with the capsule, a localized peritonitis appears which may lead to the formation of adhesions and the protection of the peritoneal cavity; or the rupture of the capsule may result in a general suppurative peritonitis. If surgical drainage is instituted or if the abscess extends along the adhesions and ruptures through the abdominal wall, there is demarcation of the necrotic tissue which separates and is discharged before healing takes place. Rarely an abscess may become encapsulated and its purulent contents thickened and calcareous.

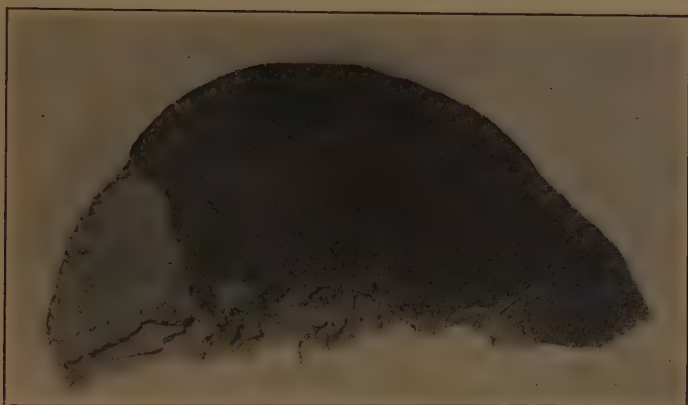


FIG. 13.—INFARCT OF THE SPLEEN. (Courtesy Prof. James Ewing, Cornell.)

Multiple minute septic emboli may lodge in the spleen in pyemic conditions and produce multiple miliary abscesses or an acute suppurative splenitis.

Chronic Inflammatory Changes.—In chronic inflammation, the changes produced are apt to differ widely depending upon the nature of the infecting agent. Generally considered, they are characterized by a primary hyperplasia of the parenchyma, chiefly of the pulp cords but also to some extent of the follicles, with a later transition to a hyperplasia of the stroma with involvement of the capillaries, vessel sheaths and trabeculae. When the fibrosis is the predominating feature of the condition, it is often called chronic interstitial splenitis. In one form or another, these chronic inflammatory changes are found in syphilis, chronic malaria, cirrhosis of the liver, splenic anemia, kala-azar and other forms of "tropic splenomegaly."

In another group of chronic infections, the lesions are granulomatous. They are found in tuberculosis, syphilis, glanders, leprosy and actinomycosis.

Tuberculosis.—Tuberculous involvement of the spleen is almost always secondary. The possibility of a primary tuberculosis of this organ will be discussed later. Secondary tuberculosis of the spleen occurs in two forms, an acute miliary process and a coarsely nodular one that is part of a more chronic type of infection.

Acute miliary tuberculosis of the spleen is a common accompaniment of acute general miliary tuberculosis which is a generally disseminated hematogenous infection. The spleen is moderately enlarged and rather firm, though occasionally soft. The surface is roughened by the presence of numerous small nodules which can be seen through the capsule as light areas (see illustration). On section, the cut surface is deep red and thickly sown with gray, grayish red or grayish yellow

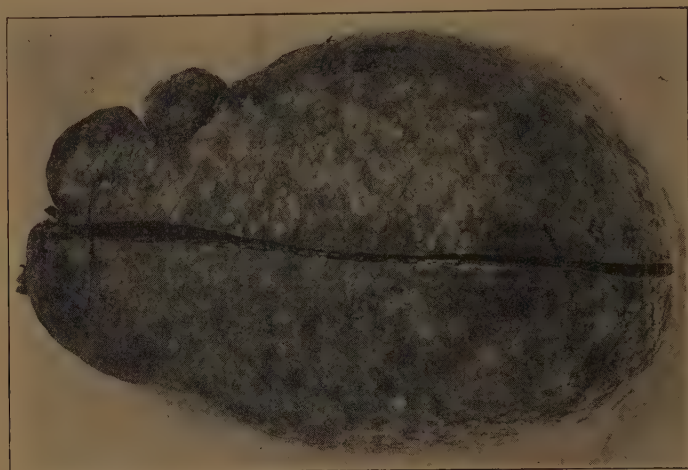


FIG. 14.—ACUTE MILIARY TUBERCULOSIS OF THE SPLEEN. EXTERNAL SURFACE. (Courtesy Prof. James Ewing, Cornell.)

nodules that measure from 1 to 6 or 8 mm. in diameter. Later there may develop more or less perisplenitis and growth of tubercles in the fibrin deposit on the surface of the spleen. When the tubercles are very small, it may be difficult to differentiate them from follicles upon macroscopic examination. Kaufmann points out that tubercles are more irregular in size and more thickly sown than follicles; that they are grayish red or yellow and translucent and are apt to be surrounded by a red zone, while follicles are gray and opaque and have no such surrounding zone; that it is easier to pick out a tubercle entire with the point of a knife, while a follicle is torn in such an attempt. Between the tubercles, the spleen tissue exhibits congestion.

In the more chronic forms of tuberculosis, the spleen is enlarged to a less extent and shows little pathologic change except for the presence of tubercles. These may vary in size from 1 mm. up to several centimeters in diameter and may be single or multiple, spherical, wedge-

shaped or conglomerate and irregular. They generally present a caseous center.

Very rarely one meets the so-called lymphoid tuberculosis in the spleen. This is essentially a hyperplastic reaction of the lymphoid tissue to the tuberculous infection and an absence of the ordinary type of tubercle with giant cells and necrosis. In the illustration it may be seen that the appearance is that of increase in the size and number of the lymphoid follicles.

In glanders, leprosy and actinomycosis, the characteristic lesions of the disease may be found in the spleen. In leprosy, they are very small, while in actinomycosis there is apt to be abscess formation. It is said that the involvement of the spleen in glanders and actinomycosis is rare.

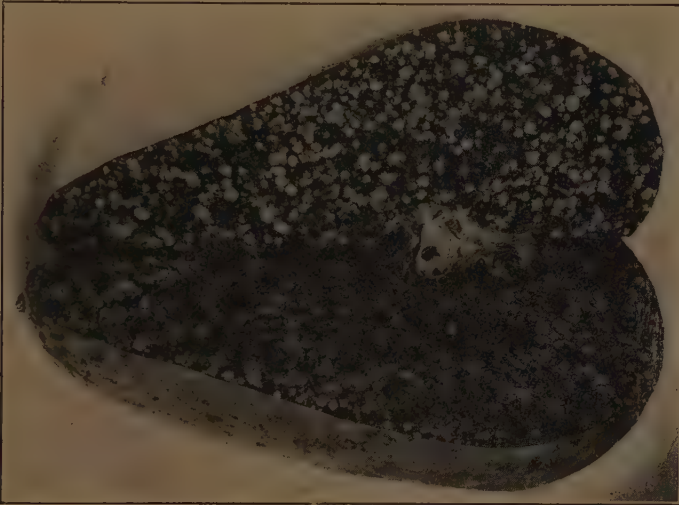


FIG. 15.—ACUTE MILIARY TUBERCULOSIS OF THE SPLEEN. (Courtesy Prof. James Ewing, Cornell.)

Cut surface of the spleen shown in preceding illustration.

Myeloid Metaplasia.—During fetal life, the spleen plays an active part in the formation of the red cells. Normally this activity ceases at or about the time of birth. In certain cases of anemia, there may take place a reversion to this embryonic method of blood formation. Whether it is a compensatory reaction because of the exhaustion of the bone marrow, or arises as a result of the action of certain toxins has been questioned by some investigators. Together with foci of formation of red cells, there are found areas in which precursors of the leukocytes are developing. Hertz claims to have demonstrated that myeloidosis of the spleen does not occur in anemia following hemorrhage, but only when there is increased destruction of the red cells, and that it may occur when the marrow is cellular and hyperplastic and shows no signs of exhaustion. Clinically the condition is seen only in chronic anemia,

which it is not possible to reproduce experimentally in animals without the use of hemolytic poisons such as toluendiamin. While it may be true that most of the forms of chronic anemia in man exhibit an increased destruction of red cells and this element is, therefore, apt to be present in any instance in which myeloid metaplasia of the spleen can be demonstrated, such a careful observer as Schridde has never seen this condition in pernicious anemia, a disease in which increased hemolysis is a prominent feature.

In myeloid metaplasia, myeloidosis or myeloidization of the spleen, as it is variously called, we find collections of myeloid cells in the venous sinuses. They consist of myeloblasts and mature myelocytes as well as large undifferentiated cells thought to be the precursors of the myeloblasts. They were at first thought to represent metastatic deposits arising in the bone marrow, but it is now believed that the fundamental cell of the myeloid series exists normally in the spleen in the form of an undifferentiated mononuclear cell which develops only in response to certain stimuli. Various authors derive these cells from the primordial lymphocyte, the indifferent adventitial cell and from the endothelium of the blood capillaries. These foci of myeloid metaplasia are, in all probability, not metastatic deposits but the cells are growing and forming in the spleen. Metastases do not lodge readily in the spleen, nests of these cells contain individuals in all stages of development and their number often bears no relation to the proportion of myelocytes found in the blood stream.

Perisplenitis.—Acute or chronic inflammation of the capsule of the spleen may arise from disturbances either within or without the organ. Abscess, infarct, chronic hyperplastic or indurative splenitis, cirrhosis of the liver and echinococcus cysticus are some of the conditions that are apt to be accompanied by a perisplenitis. A fibrinous exudate first forms over the surface and later undergoes organization and becomes transformed into hard, white scar tissue. The gross appearance of a well-marked instance of chronic perisplenitis is striking. A variable portion of the external surface of the organ is covered with a dense, white, hard layer of scar tissue. This tissue may be as hard as cartilage and measure 10 or 12 mm. in thickness. The spleen has the appearance of being covered with a layer of icing and has been called the *Zucker-gussmilz*. Sections may suggest in their appearance that the scar tissue is due to infarction, but on careful study it will be found that the spleen itself is not affected. The scar tissue of perisplenitis does not show the depression usually exhibited in old infarcts. In less extreme instances of this condition, the patches of dense hyaline tissue are small and scattered so that the color of the spleen shines through. In one case seen at the New York Hospital, this condition apparently gave rise to symptoms of pain in the abdomen. The spleen was removed by Dr. Charles L. Gibson and is illustrated here. It shows well the resemblance to an infarct.

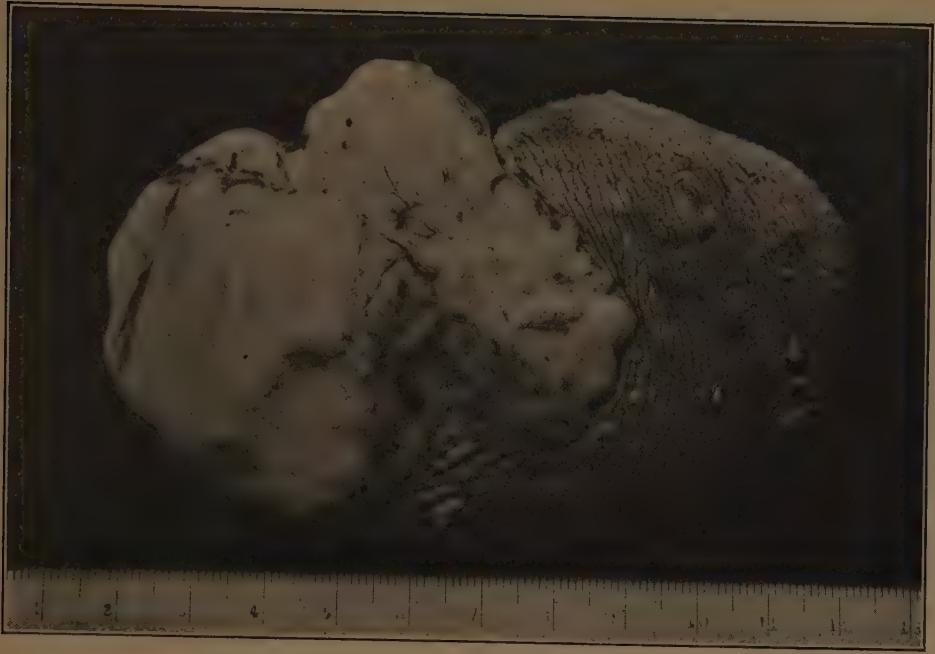


FIG. 16.—PERISPLENITIS.



FIG. 17.—CUT SECTION OF PRECEDING FIGURE. (Courtesy Dr. C. L. Gibson, N. Y. Hosp.)

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CHAPTER IV

EXAMINATION, PHYSICAL AND CLINICAL

History.—A carefully taken and detailed history is of the utmost importance as an aid to making a diagnosis in any disease and it is chiefly in this respect that the inexperienced physician is most apt to err. It is not infrequently possible to make a diagnosis with the aid of a complete history when the findings upon physical examination are not conclusive. It must be appreciated that the group of diseases associated with splenomegaly includes a number of conditions that are extremely difficult of recognition and differentiation; therefore, it may be necessary to collect every obtainable piece of evidence before a correct diagnosis can be reached.

The general physical examination of the patient should naturally be carried out thoroughly and carefully. Details of this examination will be discussed in the consideration of the several conditions which we shall study, but it will be convenient if we present at this time a brief review of those methods of physical examination which may enable us to detect an increase in the size of the spleen.

Inspection.—Upon inspection of the abdomen, it is possible to detect a mass due to an enlargement of the spleen only when the increase in size is fairly well marked. The patient should be in the dorsal position, lying with his head toward the source of light. The mass, when visible, is generally most distinctly outlined in its lower one half or two thirds and fades away under the costal margin. It usually extends from the free border of the ribs downward and toward the median line, especially in enlargements in which the whole organ is involved. In circumscribed enlargements, such as cyst or cavernous angioma, the extension of the mass may be across the upper abdomen in the direction of the liver. The shadow or outline of the mass should move with respiration.

Palpation.—Palpation is the most important method for the detection of splenic enlargement. By this means an increase in the size of the spleen may usually be recognized, especially if the enlargement is marked or if the organ is firm. On the other hand, if the organ is very soft, it may be impossible to feel it, even though it is considerably enlarged. In some instances it may be difficult to determine whether an abdominal mass is an enlarged spleen or not, and the solution of the problem may tax the capabilities of the most expert clinician.

As in every abdominal examination, it is important that the patient's abdominal wall be completely relaxed if the best results are to be

obtained. This is often strikingly illustrated in hospital patients in whom it is impossible to demonstrate a splenomegaly upon their admission. After repeated examinations the patient becomes used to the experience, the abdominal wall is relaxed and the large spleen is readily felt. A number of devices may be adopted to facilitate obtaining this relaxation. The hands of the examiner should be warm. The patient should be in a comfortable position, generally with the thighs somewhat flexed. He should be instructed to breathe deeply through the open mouth. In nervous, sensitive persons it is sometimes helpful to engage

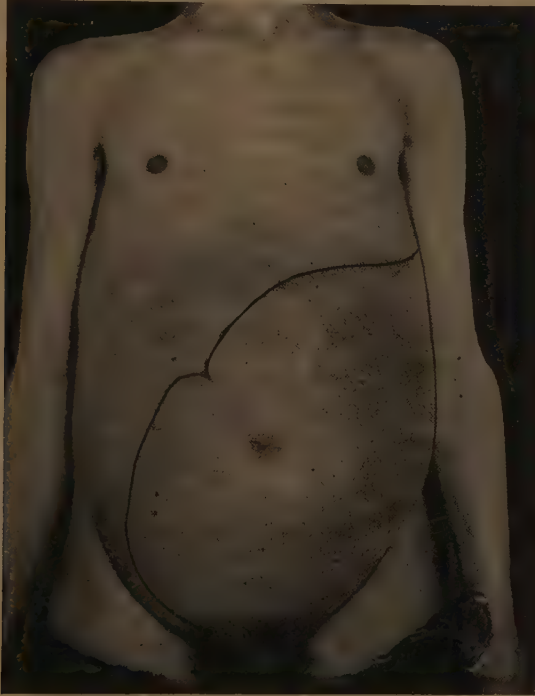


FIG. 18.—ENLARGEMENT OF ABDOMEN AS THE RESULT OF A LEUKEMIC HYPERTROPHY OF THE SPLEEN. (From Eisendrath, *Surgical Diagnosis*.)

them in conversation during the examination. Palpation should be made slowly and easily, and, if there are tender areas, these should be palpated after the rest of the abdomen has been thoroughly examined. As a general rule it may be said that the more intelligent the patient, the easier it is to secure an absence of voluntary spasm of the abdominal muscles.

Gentleness should be exercised in all cases, but this is especially true when the organ is large and soft, as in acute infections. With vigorous palpation it is possible to produce a rupture of the organ or of surrounding adhesions and this may lead to serious hemorrhage or infection. Many methods have been followed in the palpation of the spleen and we

shall not attempt to give all of them. Each has its adherents and it is probable that each examiner obtains the best results with the method with which he is most familiar.

A useful method for the demonstration of slight enlargements is recommended by Calambos. In his opinion, palpation with the fingers directed downward rests upon a physiological basis and yields decidedly better results than palpation from the front, especially when the abdominal coverings have been properly relaxed. His method is as follows: The patient is placed in the dorsal position with the thighs flexed. The physician stands at the left side of the bed. His left hand presses upon the abdominal wall at approximately the level of the umbilicus, and is



FIG. 19.—SARCOMA OF SPLEEN—DOTTED LINES. (From Eisendrath, *Surgical Diagnosis*.) Observe notches on right margin. Well-marked caput medusæ.

moved slowly toward the left hypochondrium, while the hooked fingers of the right hand palpate under the costal arch. In favorable cases, it is possible to palpate not only the margin but also the diaphragmatic, gastric and colic surfaces of the lower portion of the spleen, whereas with the customary methods the diaphragmatic surface only can be examined, the lower border being felt less distinctly and the gastric and colic surfaces not at all. In palpating with the palmar surface of the hand, the physician succeeds in slipping his fingers under the lower border of the spleen so that the colic surface of the organ comes to lie over the terminal phalanges. Thorough relaxation of the abdominal walls may be obtained by pressing down upon the abdomen with the free hand at some distance from the spleen and, at the same time, sweeping it cau-

tiously nearer to that organ. By means of this procedure, the portion of the abdominal coverings situated between the two hands becomes relaxed and flaccid with the result that it is more accessible to palpation, carried out with the volar surface of the fingers.

Cabot recommends palpation from the front. The patient should be on his back with his head comfortably supported and his thighs flexed. The physician stands at the right side of the bed facing the patient. The palm of the left hand is placed over the normal situation of the spleen and draws the whole splenic region downward and inward toward the finger tips of the right hand; at the same time it should slide the skin and subcutaneous tissues over the ribs and toward the right hand so as to leave a loose fold of skin along the margin of the ribs and give the palpating fingers a slack rather than a taut covering to feel through. The right hand lies on the abdominal wall just below the margin of the ribs, and the fingers point straight up the path down which the spleen is to move, that is, obliquely toward the left hypochondrium. With the hands in this position, the patient is asked to draw a full breath. Near the end of inspiration the hands are drawn slightly toward each other and a little dip is made with the right finger tips so that, if the spleen issues from beneath the ribs, its edge will meet the finger tips for an instant and spring over them as they rise from diving into the soft tissues.

The right lateral position, an intermediate position and also the vertical position have been recommended for palpating the spleen, but one of the two methods given above are used regularly by the majority of physicians and can be depended upon to give good results when carefully applied.

By palpation, an attempt is made to determine the position, size, shape, consistence, mobility and sensitiveness of the spleen. It is generally agreed that the normal spleen is not palpable. If the organ can be felt, it may justifiably be considered enlarged or displaced. Its position and shape should be carefully noted. Deviations from the normal shape are produced by circumscribed enlargements such as are met with in abscesses, cysts or tumors of the organ. If the anterior border can be felt, it should usually be possible to recognize the notch or notches in it, and, by this means, to identify a mass as the spleen, even should it be situated far from its normal position. But exceptions to this rule have been described. The consistence is rated as soft, firm or hard depending upon the sensation transmitted to the examining fingers. Normally it is firm. In general, the acute enlargements are soft, while the chronic are hard.

Normally the spleen moves downward with the excursions of the diaphragm, and this movement may be recognized in the presence of splenomegaly unless the greatly enlarged organ is firmly fixed by adhesions or reaches into the pelvis and its movement is checked by contact with the pelvic bones. Its mobility may also be established by manipulation with change in position of the patient and also by ballottement

from behind (Hartsmann). This latter form of mobility may be interfered with by the presence of adhesions. It is said that adhesions may at times give a sensation as of crunching snow. Pain may be elicited in certain conditions, such as acute splenitis, by pressure upon the spleen.



FIG. 20.—SPLENIC DULLNESS IN SPLENOMEGALY OF MODERATE DEGREES. (From A. Weil.)

Percussion.—Percussion is of relatively little value in determining the size of the spleen. Normally, there is dullness in the midaxillary line from the ninth to the eleventh ribs, corresponding to that portion of the organ which is most superficial. Its lower and posterior borders cannot be defined. Its anterior edge of dullness is approximately in the

anterior axillary line. If this small area of dullness is enlarged upward and forward, and if the edge has been felt below the ribs, it is probable that the increased area of dullness corresponds to an enlargement of the organ (Cabot).

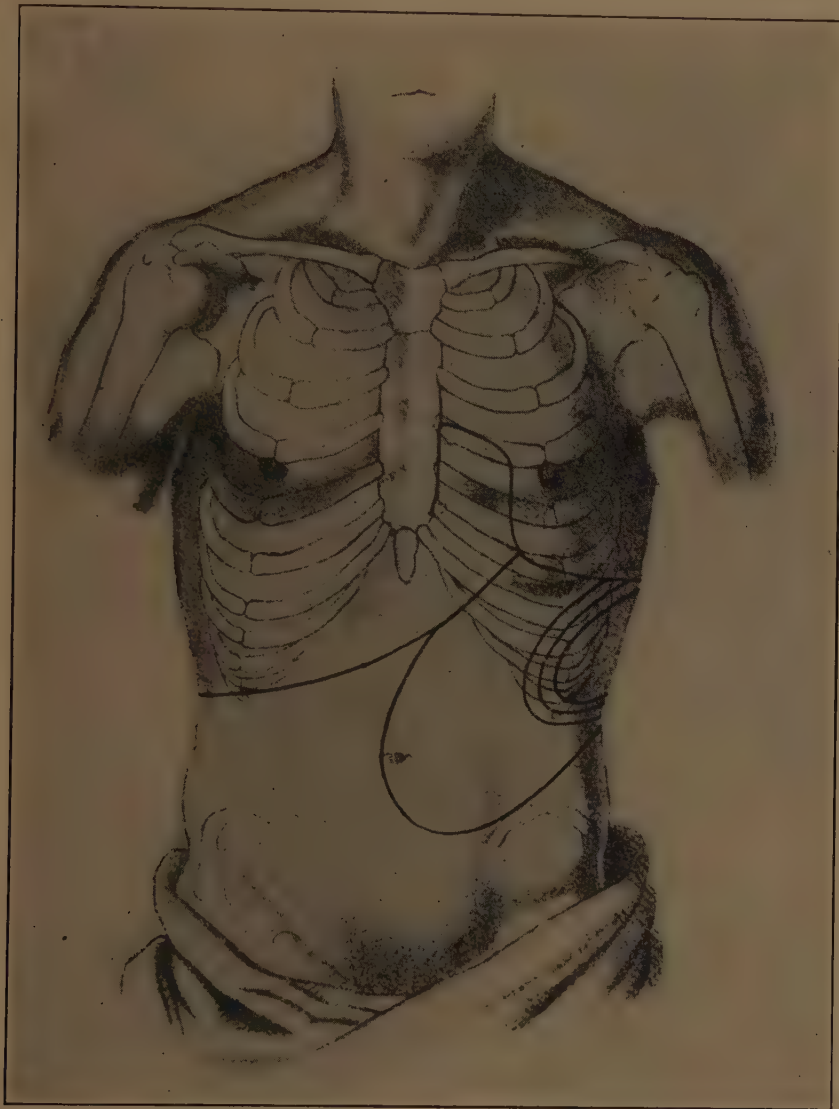


FIG. 21.—SPLENIC DULLNESS IN SPLENOMEGALY OF VARIOUS DEGREES. (From A. Weil.)

Auscultation.—Auscultation yields but little information. A souffle, first described by Roser in 1862, occurs at times in splenomegaly. It is said to be soft and systolic and not affected by the position of the patient. Auscultatory percussion can do little more than extend somewhat the recognizable area of dullness.

Inflation of Adjacent Viscera.—In the presence of a mass in the left hypochondrium, it is sometimes difficult to determine whether it consists of spleen or kidney. In such a situation it is sometimes of assistance to inflate either the stomach or the colon with air. The spleen is very superficially placed so that the inflated colon will pass behind it and produce no change in the area of dullness. On the other hand, the inflated colon will pass in front of an enlarged kidney and thus diminish the area of dullness produced by it. Inflation of the stomach will tend to diminish the area of dullness found over a spleen that is normal, or but slightly increased in size, but may have no influence upon the dullness found over a greatly enlarged spleen.

Exploratory Puncture.—In chronic splenomegaly and in many acute infections, valuable information can be obtained, no doubt, by the examination of material collected by puncture of the spleen. The fact that typhoid bacilli, malarial parasites and the spirochetes of syphilis and relapsing fever accumulate to a great extent in this organ shows how much evidence can be obtained by means of such a procedure. Schupfer and Florence devised a punch which they used to remove bits of tissue for microscopic examination. For some time puncture of the spleen was done quite frequently as a diagnostic measure in a variety of conditions, but there soon accumulated reports of undesirable results so that the procedure fell into disrepute. Laceration of the capsule and fatal hemorrhage have occurred after puncture, and peritonitis has resulted when the spleen was the site of suppurative splenitis or abscess. Developments in bacteriological methods, such as the blood culture and the agglutination tests (Widal), have rendered splenic puncture unnecessary in typhoid fever and many of the acute infections. Advances in our knowledge of the pathologic morphology of the blood have largely superseded this procedure in the diagnosis of the so-called blood diseases. In abscess of the spleen it is both advised and condemned (Spear, Melchior). At the present time the physician is less liable to find himself dependent upon puncture of the spleen as a means of substantiating a diagnosis, though it may be said that the method seems to be gradually gaining in favor again, especially in the diagnosis of kala-azar in which it appears to be relatively safe. Puncture of the spleen is less justifiable in the acute infectious diseases in which the organ is large, soft and friable. It is said that it may be done without danger if the spleen is hard, as it is in chronic malaria. If puncture is elected, all preparations must be made for abdominal section, should indications appear demanding surgical interference. The technic is thus given by Morrow:

The site of the puncture is through the tenth intercostal space in the mid axillary line on the left side, or, if the organ is much enlarged, some point below the costal margin over the spleen. The skin is anesthetized and a small nick made in it with a scalpel. The patient is directed to hold his breath and a long, fine, aspirating needle is quickly inserted, the aspiration made with as little delay as possible, the needle

withdrawn and the site of the puncture sealed with collodion. The patient should be kept perfectly quiet for at least twenty-four hours afterwards.

Roentgen Ray.—Examination of the abdomen in the usual manner by means of the Roentgen ray, whether with the fluoroscope or with photographic plates, rarely gives much information as to the size of the spleen in ordinary cases of splenomegaly. In cases of cyst, abscess or

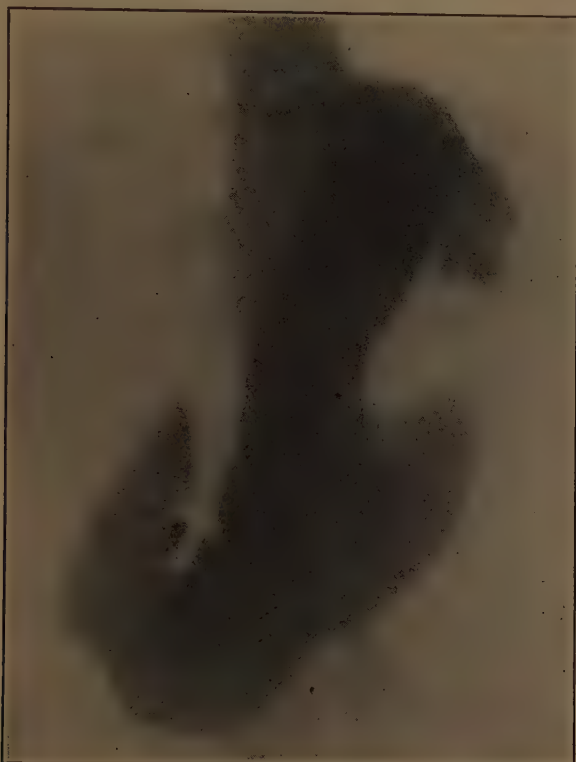


FIG. 22.—X-RAY OF STOMACH AFTER INGESTION OF BARIUM. (Courtesy Dr. A. V. S. Lambert, *Annals of Surgery*.)

Note irregularity of outline due to pressure of large cyst of spleen.

tumor, there may be some shadow that will help in the diagnosis (*cf.* Fig. XXII). The position of the diaphragm is of course indicated, but beneath it there are generally no recognizable details. Additional information as to the site, position and size of the spleen may be obtained in appropriate cases by the use of the X-ray after inflation of the abdominal cavity with oxygen or air. This procedure has been introduced comparatively recently in this country by Stein and Stewart, and has not been practiced sufficiently to permit final judgment as to its value, but several investigators have found it helpful. Some pain and discomfort may follow inflation of the peritoneal cavity, but, so far as

has yet been ascertained, the procedure is harmless. In one of our cases it was used with satisfactory results. It was shown that the spleen was small, not fixed by adhesions, and that it contained certain opacities.

In another instance the information obtained by this procedure was not as satisfactory, though at the time of operation it was proved to be accurate. The patient, male, twenty-seven, suffering from pain in abdomen, presented an obvious abdominal mass extending across the upper portion of the abdomen. The lower border was well defined and crescentic.

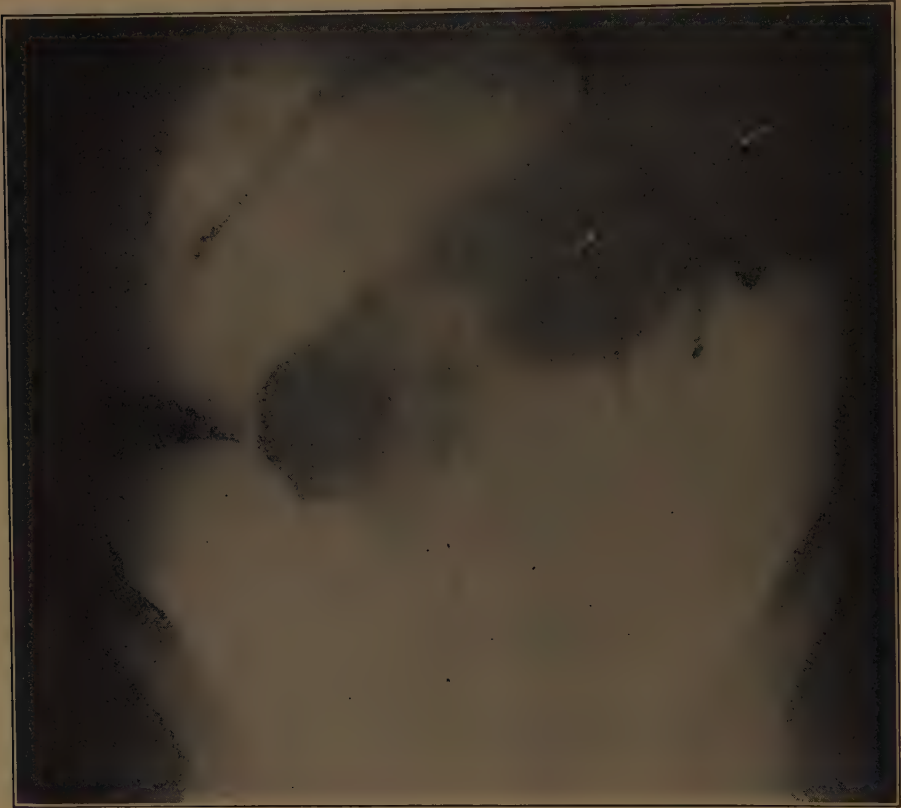


FIG. 23.—SHOWING PRESSURE ON DESCENDING COLON BY LARGE SPLEEN OF SPLENIC ANEMIA.

Beginning at the costal margin, in about the right mammary line, it curved downward and to the left, crossing the midline at about the level of the umbilicus. From there it curved upward to the left hypochondrium. At the termination of this border in the splenic area, the mass appeared to be separated from a much smaller one by a notch or space. The lower border of the smaller mass felt like the border of a normal or slightly enlarged spleen. It was impossible satisfactorily to determine by palpation whether the large mass was spleen or was connected either with the spleen or the liver. The patient's peritoneal cavity was inflated with oxygen and X-ray plates made. These showed

that the liver was normal in size and that the mass in question was probably not connected with it. In the splenic region, there was the appearance of a small spleen-shaped shadow resting upon the upper extremity of a larger mass and possibly, though not clearly, connected with it.



FIG. 24.—OXYGEN INJECTION SHOWING LARGE SPLEEN. (Courtesy Dr. W. H. Stewart.)

The operation showed that the entire mass was made up of spleen weighing 1,500 gm. which had extended across the midline in the upper abdomen (an unusual direction for the extension of an enlarged spleen). There was a lobulation at its upper extremity. The lobule, partially separated, was of about the size of the normal spleen and was connected with the main bulk of the organ by a bridge of tissue 6 cm. in diameter

(*cf.* Fig. XXV). The plates had given a correct image, and correct interpretation would have yielded a correct diagnosis.

In cases in which there is doubt as to whether a mass is due to enlargement of the spleen or of the kidney, it will be advantageous to make an X-ray examination with ureteral catheters in place and, after distention of the renal pelvis (left) with some solution which is opaque to the Roentgen ray.

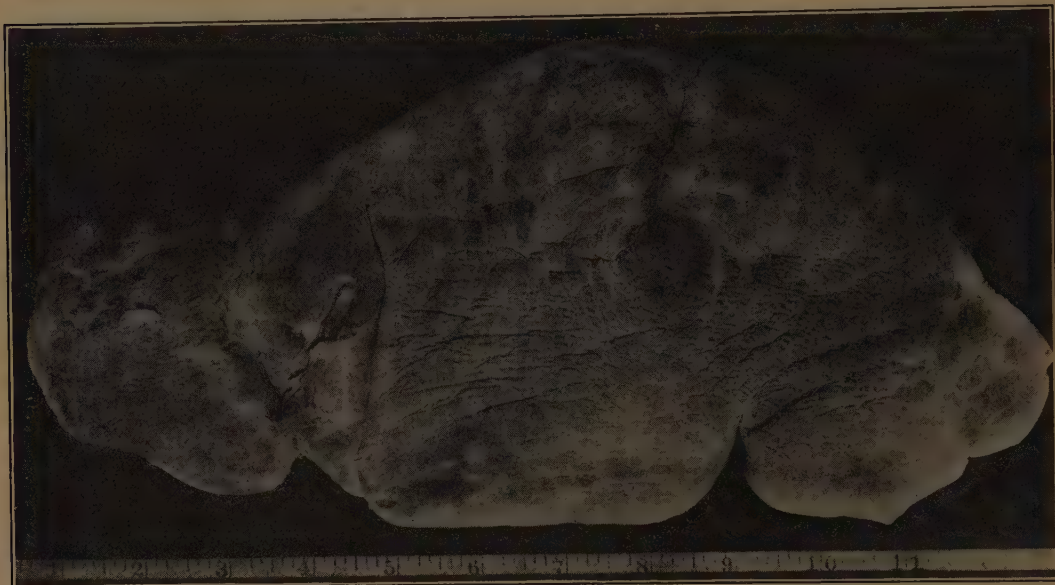


FIG. 25.—SPLENIC ANEMIA.

Spleen removed at operation. The lobule at upper pole is bent on itself showing only about half of its breadth.

Splenic Opacities.—Opacities in the splenic area are occasionally noted in X-ray plates, yet few references to the subject are found in the literature.

We observed such a condition in a young woman who had suffered discomfort in the left hypochondriac, lower costal and lumbar regions for about one year. Some hematuria was said to have been noted and X-ray plates showed opacities which seemed at first to be in the kidney. A complete examination, including catheterized ureteral specimens, failed to reveal anything abnormal in the kidney. Plates taken after injection of the pelvis of the left kidney showed the opacities to be outside of the kidney, the outline of which was distinguishable. It was then inferred that the opacities were splenic, possibly tuberculous, and that the pain might be due to adhesions. Accordingly oxygen was injected into the peritoneal cavity. This demonstrated that the spleen was not fixed by adhesions and was small. The opacities (Fig. XXVI) were likewise demonstrated to be in the spleen. The findings

did not seem to warrant operation. The patient improved and reported two years later that her health was good and the pains had ceased.

Mitchell reports having seen four or five cases *intra vitam*, and on two occasions has found numerous calculi postmortem. He gives the details of one case in which he examined a spleen recently removed from the body. The shadow-producing bodies were hard calculi firmly embedded in a fibrous capsule. Analysis showed them to consist of 67.7 per cent calcium carbonate. The spleen was from a man sixty-seven years of age, otherwise healthy, who died of anthrax. The probability is that these foci were healed tuberculous nodules. Mitchell sug-

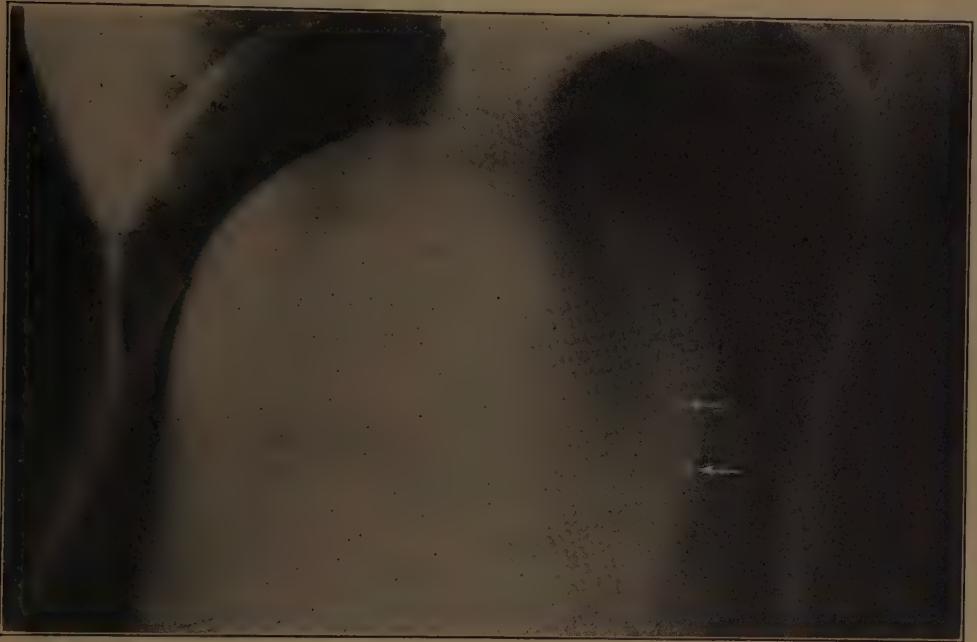


FIG. 26.—PNEUMOPERITONEUM.
Note spleen and splenic opacities.

gests this as a possibility. Klotz's findings, referred to under tuberculosis of the spleen, add weight to this view.

Examination of the Blood.—The examination of the blood is of prime importance in all cases of splenomegaly. In a number of instances the diagnosis can be made in no other way, while in all of them the information thus acquired will be of value in determining the cause of the trouble, influencing the treatment and estimating the prognosis. Deviations from the normal constitution of the blood naturally differ in the various conditions which we shall discuss, and the details in each instance will be described in their appropriate place. At this time we shall merely discuss, in a general way, the method of examinations which may be made, their technic and significance. The importance of

accurate blood examinations in connection with numerous diseases which demand surgical intervention, and also the frequent references which will be made to blood findings, indicate a rather detailed presentation of this phase of the physical examination.

Hemoglobin.—The estimation of the hemoglobin percentage is the first examination to be made, especially since anemia is apt to play an important part in diseases of the spleen. The estimation is done by various methods that are on the whole satisfactory, but it has become the practice to record the result as a percentage of the normal without reference to the value of 100 per cent expressed in terms of actual hemoglobin content. Several standards have been proposed, based upon the examination of healthy persons in different parts of the world. Sahli's figure of 17 gm. of hemoglobin per 100 c.c. of blood was obtained by using the blood of Swiss mountaineers and is generally accepted as being too high. Meyer and Butterfield obtained figures of 16.6 gm. for males and 15.0 gm. for females in Munich, but their figures have not found general acceptance. Haldane, in England, found 13.8 gm. of hemoglobin per 100 c.c. to represent the normal, and the standard used in this country generally conforms to his results. Apparently no one has made an extended study of the hemoglobin content of the blood of normal persons in this country, but it is highly probable that it would vary greatly in different places depending upon the nutrition and environment of the persons examined, the altitude of the locality in which they live, the climate and their occupation. It is most desirable that a uniform standard be accepted throughout the world as corresponding to "100 per cent of hemoglobin" or, better, that hemoglobin estimations be reported as gms. per 100 c.c. of blood.

Methods.—The simple and old Tallquist book has been frowned upon for so long that it requires some courage to say a good word for it. But if it is used carefully and read promptly with good daylight falling upon the book from behind the observer, it gives results that are quite dependable. It is readily read to intervals of 5 per cent, which is probably as close a reading as can be obtained with most methods.

The Dare hemoglobinometer is representative of those instruments which utilize a wedge-shaped ruby glass as a standard. It is convenient in its manipulation and satisfactory, but it is expensive and the highest accuracy in its use can be obtained only by making the reading in a dark room by candlelight. Since the colors are dissimilar, they compare differently when illuminated by another source of light than that for which the instrument was designed.

Methods in which the hemoglobin is changed to carbon monoxid hemoglobin and compared with a standard solution of the same substance have been used, especially in England. Palmer, in this country, has perfected the method and devised a standard which he claims will remain unaltered for one year. We have had little experience with these methods.

The Sahli method is an example of those which change the hemoglobin of the blood to acid hematin and compare it with a standard of the same substance. When used properly, the method is quick, simple and reliable. But there are several objections to it. The standard color tubes which are furnished with the instrument are not permanent and must be replaced or restandardized from time to time, even in the case of the new Küttner tubes for which the claim of permanency was made. It is not generally appreciated that the acid hematin color does not develop fully until twenty-four hours after the addition of the blood to the decinormal acid. Sahli directed that the readings be made at the end of five minutes and some teachers in this country have advised a three-minute interval when using the standards made in the United States. Newcomer has studied the question and has been able to devise a formula whereby a correction can be made to allow for this slowness in color development. This formula is $xy = -40$, where x is the time in minutes elapsing between the addition of the blood to the decinormal hydrochloric acid and the reading; y is the percentage by which the maximum color of the mixture has failed to develop.

$$\frac{40}{\text{time in minutes}}$$

therefore gives the figure that is to be added to the reading. In our hands the Sahli method has been satisfactory, provided Newcomer's time element factor is always employed and provided the standard tubes are restandardized about once every three or four months.

Newcomer has introduced a modification of the acid hematin method that is highly accurate. By careful search, he has found a glass that has practically the same absorption spectrum as acid hematin and, therefore, provides an unfading standard with which mixtures of blood and hydrochloric acid may be compared. This glass is interposed above one of the prisms of the Dubosq colorimeter or similar instrument, the blood acid mixture is placed in the chamber under the other prism and readings are made. By means of a set of tables which vary for the thickness of the glass used, the number of gm. of hemoglobin per 100 c.c. of blood can be obtained. Of course this is not a clinical method, but it is admirably suited to the purpose of standardizing Sahli color tubes.

Van Slyke's method of determining the hemoglobin content of the blood by measuring its capacity to combine with oxygen is probably the most accurate of all, but it is convenient only in well-equipped laboratories.

We are inclined to recommend the Sahli method for accurate work. Mixing in the graduated tube without loss of fluid and consequent error is facilitated by the use of a soft rubber stopper. The Küttner tubes are made of such a strength that 100 per cent corresponds to a hemoglobin content of 13.8 gm. per 100 c.c. of blood. Where the hemoglobin content of the blood falls below 2.7 per cent (20 per cent of normal) it is desirable to use twice the amount (that is, 40 c.mm.) of blood and twice the amount of acid that is ordinarily used.

Red Cell Count.—The number of erythrocytes in the blood is estimated in the usual manner, using a 1:100 diluting pipette and 0.9 per cent sodium chlorid, Hayem's solution or Toison's solution as the diluting fluid. It should be remembered, in using the Buerker type of counting chamber which has become so popular recently, that counts should be made as rapidly as possible to avoid changes brought about by evaporation. Five million red cells per c.mm. are considered the normal figure for males and four and one half million for females.

Color Index.—The color index expresses the relation between the percentage of red cells and that of hemoglobin, that is, the hemoglobin content of the average red cell. It is found by dividing the hemoglobin content expressed as percentage of normal (100 per cent) by the red cell count expressed as percentage of normal (5 million). The color index is normally 1.0. It is reduced in secondary and chlorotic anemias, while in the pernicious group of anemias it is comparatively high, being greater than 1.0 in a large percentage of the cases. An accurate determination of the color index depends naturally upon the accuracy of the red cell count and the hemoglobin estimation.

White Cell Count.—The number of white cells in the blood is estimated in the usual manner using a 1:10 diluting pipette and 1 per cent acetic acid with or without some dye as a diluent. We do not recommend the use of Toison's fluid as a diluent, although, by using it, it is possible to make both red and white cell counts in the same preparation. The presence of both red and white cells in the mixture tends to confuse the examiner and to increase the time necessary for making the count. It should be noted that the white cells tend to agglutinate in the acetic acid diluent and that, in order to obtain a proper distribution of cells in the fluid, the pipette should be shaken for two minutes before the drop is placed in the counting chamber. In this method, there is estimated not only the white cells, but all of the nucleated cells of the blood, so that if erythroblasts are present it is necessary to correct the white cell estimation by determining the percentage of the nucleated red cells among the nucleated cells found in a stained film.

While in general it is said that the white cells in the blood normally number 5,000 per c.mm., it is known that they vary widely under normal conditions, and it has become the practice not to speak of a leukocytosis unless the white cells number more than 10,000 per c.mm. Physiologic leukocytosis occurs during the course of digestion, in infancy, during pregnancy, after cold baths and after exercise. It is important, therefore, that these factors be considered in the interpretation of any leukocyte count.

Morphological Study.—The critical examination of the stained blood film is often one of the most difficult and, at the same time, one of the most instructive procedures that we can apply to the blood. The experienced observer can frequently render his opinion after examination of a properly made and stained film in the absence of hemoglobin estima-

tion and cell counts, but this practice should be permitted only to the expert hematologist. The average examiner desires all the evidence possible before he makes his diagnosis. Microscopic examination of the fresh blood has its place in the detection and recognition of parasites, but is now rarely resorted to in other conditions.

Blood films may be made upon slides or cover-slips according to the various technics described in the textbooks. It is generally said that there is a more even distribution of the white cells in films spread upon cover-slips than upon slides, and it is true that in many instances of slide preparations one finds the large mononuclear and transitional cells, and, to a somewhat less extent, the polynuclear neutrophils, in greater numbers at the edges and ends of the film. But it is possible to make the films so carefully that slide preparations are as good as cover-slip spreads, and comparative counts of the two have closely approximated each other (Thro).

For the ordinary "surgical leukocyte and differential," in which there is desired only the percentage of polynuclear cells, it is a rapid and accurate procedure to count the cells in the counting chamber in the same preparation as that in which the white cell count is made, using the high power dry objective for the purpose. For routine differential counts and for the study of the morphology of individual cells, slide preparations are to be preferred. Cover-slip films should be used whenever a highly accurate numerical differential count is desired. The importance of exact numerical differential counts is often greatly exaggerated. The significant elements are the presence of abnormal cells and the general aspect of the picture presented. A differential count should never be based upon a count of less than two hundred cells and usually should depend upon an examination of from three hundred to five hundred white cells.

Any good Romanowsky stain will give a satisfactory preparation for morphological study. Formulae devised by Jenner, Wright, Hastings, McJunkin, Leishman and Giemsa are in general use and it makes but little difference which one is used, provided a satisfactory sample can be secured. Much of the trouble with blood stains since the War has been due to the poor quality of the methyl alcohol used. It is possible to purchase satisfactory stains in this country at the present time from many dealers. It is important that the directions for using the stain selected should be followed exactly, for deviation from them has led to much dissatisfaction. Pappenheim's so-called panoptic stain may be recommended when a careful study of the morphology of individual cells is desired. It requires more time and trouble than other stains but gives very beautiful pictures.

In normal blood, the red cells appear as evenly stained round cells, all of nearly the same size and none containing a nucleus. Deviation from the round shape, known as poikilocytosis, was one of the first changes noted in the erythrocytes in pernicious anemia. It was quite

obvious in diluted blood under the lower power objective of the microscope and was recognized before the introduction of the modern staining methods. Deviation from the uniform size is known as anisocytosis and is evidenced by the presence of both small and large erythrocytes. The presence of definite megalocytes, large non-nucleated red cells, may be the only evidence in the blood of a pernicious anemia during the stage of a remission. Very small cells are believed to be portions of cells that have undergone fragmentation in the circulation. Departures from the normal staining reaction are of two kinds. When the color index is low, the center of many of the cells is stained poorly or not at all, leaving the so-called central pallor. In some forms of anemia, especially when the color index is high, the red cells take up some of the basic elements of the stain and appear more or less bluish. This is known as polychromatophilia and is an indication of the youth of the cell. It is well marked in the megaloblasts and, in the most primitive forms, attains such an extreme degree as to render their differentiation from lymphocytes a matter of some difficulty.

Nucleated red cells are always abnormal when found in the circulating blood. They occur as normoblasts or megaloblasts. Normoblasts are of about the same size as the normal red cell and do not usually show polychromatophilia. The nucleus is typically pyknotic and often appears to be dividing. Megaloblasts are generally larger than the normal erythrocyte but may be of the same size. The cytoplasm often shows more or less polychromatophilia and the nucleus is comparatively large and shows a radial structure. The most primitive forms of megaloblasts have a basophilic cytoplasm containing but little hemoglobin and, as pointed out by Butterfield and Stillman, are apt to be mistaken for lymphocytes. If the two forms of cell are viewed side by side, it can be seen that the cytoplasm of the lymphocyte stains a pure blue while that of the megaloblast has a slaty color indicating the presence of some red dye in the cell. Basophilic stippling, the so-called granular degeneration of the red cells, is seen as fine blue dots scattered through the cytoplasm. It occurs in both the nucleated and the non-nucleated cells and is found in many forms of anemia. It has been claimed that the stippling found in the erythrocytes in lead poisoning is in part due to the actual deposition of lead in the red cells and is not the same in character as that found in the usual cases of anemia (McJunkin).

Cabot's ring-bodies are delicate threads in the form of rings or figure-of-eights. They take a violet stain with Giemsa and are thought to be the remains of the nuclear wall. Howell-Jolly bodies are larger than the granules of basophilic stippling and take a basic stain. They are considered to be nuclear rests. Both of these structures are found in various forms of severe anemia and are evidence of the youth of the cell.

The differential count of the varieties of white cells in the blood film is made as a matter of routine, although, as has been said above, the

exact numerical values thus obtained are not often of much value in reaching a diagnosis of the conditions which will be discussed in this paper. Films for this purpose are preferably made upon cover-slips for highly accurate work, though slides may often be used to advantage. In normal blood, the percentages of the different types of cells vary within rather wide limits. Naegeli gives the following figures:

	Per cent
Polymorphonuclear neutrophils	65-70
Polymorphonuclear eosinophils	2- 4
Basophils or mast-cells of the blood	0- $\frac{1}{2}$
Lymphocytes, both large and small	20-25
Large mononuclears and Ehrlich's transitional cells (Mc-Junkin's endotheliocytes)	6- 8

There will be little difficulty in recognizing the normal white cells in the film. In considering the abnormal cells that one may see, it is well to remember that, in their development, the cells of the granular series (represented by the polymorphonuclear leukocytes of normal blood) pass through gradual changes from one form to another and that many names have been given to the various individuals seen at the several stages during this process. Thus we have the primordial leukocyte, the myeloblast, the promyelocyte, the myelocyte, metamyelocyte and finally the polynuclear leukocyte of normal blood. It should be understood that, in the study of a film of blood in which there are many abnormal leukocytes, one is apt to find cells which do not fit any of the classifications in general use. It is sufficient to recognize that these cells are immature members of the granular series and it is unnecessary to name them exactly. Metamyelocytes differ from polynuclears only in that they have a horseshoe-shaped nucleus instead of the polymorphous form, and are found to some extent in normal blood. Cells that occur earlier in the series than the metamyelocyte are not normally found in the circulating blood and when present indicate pathologic stimulation of the bone marrow. It is known that in children less stimulus is needed to induce the appearance of these cells in the peripheral blood stream than is the case in adults. Pathologic lymphocytes are found less often, generally in cases of lymphatic leukemia. Plasma cells, Türck's irritation or stimulation forms, megakaryocytes and splenocytes are found at times. The significance of these forms is not at all clear, but they are considered to indicate pathologic activity on the part either of the bone marrow or the lymphoid tissue. Attempt has been made to differentiate between cells of the myeloid and lymphoid series by the use of the "oxydase" staining reaction of Schultz. While not invariably successful it is sometimes helpful.

Blood-Platelets.—It is occasionally possible to recognize a marked increase or decrease in the number of platelets in the examination of the stained film. Actual counting of these structures is the only satis-

factory way of determining a deviation from the normal number. The method of Wright and Kinnicutt is the best that has been devised, though one recently introduced by Gram offers many advantages. The platelets normally range between 200,000 and 500,000 per c.mm. They play an important part in the process of coagulation of the blood and are diminished in purpura hemorrhagica and some other conditions in which the coagulation and bleeding times are prolonged (Duke).

Vital Staining.—By the so-called “vital staining” methods, one demonstrates the reticulated erythrocytes. These cells are present to the extent of about 0.8 per cent in normal blood and are increased in various forms of anemia, especially when there is an increase in blood destruction. A number of methods have been proposed for their demonstration. A method that has proved satisfactory in our hands was introduced by Widal and his coworkers. Four to six drops of blood are added to a centrifuge tube containing about 10 c.c. of a 0.2 per cent solution of potassium oxalate in 0.1 per cent sodium chlorid and ten drops of Unna’s polychrome methylene blue. The contents of the tube are well mixed, allowed to stand for ten minutes, centrifuged and the supernatant fluid poured off. The cellular sediment is smeared upon slides, fixed with heat and examined with the oil immersion lens. A certain number of cells are found to contain a purplish, violet or bluish skein or reticulum. The earlier observers of these cells found them much increased in hemolytic jaundice and thought they were the “sick cells” or the more fragile red cells. Later writers showed that the reticulum is rather a sign of youth than of fragility and the percentage of these cells in the blood is considered a reliable indication of the hematopoietic activity of the blood-forming organs. Key believes the reticulum is the result of the union of the vital stain with a basophilic substance characteristic of young cells. Cunningham has recently reviewed the methods for staining these reticulated cells and proposes an excellent method by the use of which permanent preparations may be obtained.

Erythrocyte Fragility.—In some forms of anemia in which hemolysis is increased, it has been demonstrated that the red cells are more fragile, that is, more susceptible of hemolysis than is normally the case. This fragility has been demonstrated by the use of several hemolytic agents such as saponin and hemolytic immune sera, but hypotonic solutions of sodium chlorid are most generally used. Blood is drawn into 1 per cent sodium chlorid containing about 0.5 per cent potassium oxalate to prevent clotting. The cells are washed three times by centrifugation in 0.9 per cent sodium chlorid and, in the final centrifugation, are sedimented into as compact a mass as possible. The supernatant fluid is pipetted off as completely as possible so that the cells may be free from salt solution. A series of small test-tubes is set up and to each is added a succession of dilutions of sodium chlorid beginning at about 0.70 per cent and running to 0.30 per cent with a difference of 0.02 per cent

between each two adjacent tubes. This is most conveniently done by adding separately to each tube calculated amounts of 0.7 per cent sodium chlorid and distilled water and then mixing them. If the volume of solution in each tube is 3.5 c.c., the calculation is simple. To each of these tubes is next added one drop of the washed red cells from a capillary pipette and the tubes gently inverted twice to mix their contents. The tubes are allowed to stand at room temperature from ten to fifteen minutes and then centrifuged for about three minutes to sediment the cells. The supernatant fluid is examined for the first trace of hemolysis, which will appear as a slight yellowish tinge. Complete hemolysis is said to occur in the first tube beyond which there is no deepening of the red color, that is, where there are no intact cells in the sediment. It has been recommended that, instead of centrifuging the tubes, they be placed in the ice box for twenty-four hours, to allow the cells to sediment by gravity, but the method described has proved satisfactory in our hands. In normal blood, hemolysis begins at about 0.44 per cent and is complete at about 0.32 per cent, sodium chlorid. In the more severe forms of hemolytic icterus, hemolysis may begin at 0.70 per cent and be complete at 0.55 per cent. It has been said that it is not necessary to wash the red cells in preparation for this test and certainly the procedure of washing may be expected to cause some change in the cells. But if they are not washed, the presence of elements of the serum may introduce complications that are not well understood. If saponin is used as the lytic agent, washing is necessary, for the serum contains substances that protect against the action of saponin. Should hemolysis appear during the washing, it is wise to obtain a fresh specimen of blood and wash it with a stronger solution of salt such as 1.2 per cent or 1.5 per cent. In a satisfactory test, the tubes should show a gradual and even change of color from one extreme to the other.

Coagulation Time.—The determination of the clotting time of the blood is an essential procedure in those cases which show a tendency to hemorrhage, especially if an operation is considered. The methods for estimating the coagulation time are numerous and the time for normal bloods differs according to the method used. Cohen has reviewed the various methods and shows that the normal coagulation time may vary between three and thirty-five minutes, depending upon the technic. The Bogg's coagulometer is a simple and satisfactory instrument. Duke and Cohen have devised modifications of Milian's method which require little apparatus and give sharp end points. McGowan's method, which depends upon the use of capillary tubes, is satisfactory and simple if the proper tubes are at hand. When estimated by these four methods, the normal clotting time is found to be between three and eight minutes. Any marked delay in the coagulation of the blood constitutes a warning against operation without the institution of measures designed to prevent hemorrhage. For the latter purpose, transfusion of whole

blood, injection of serum, injection of solutions of sodium citrate and X-ray irradiation of the spleen have been recommended.

Bleeding Time.—Duke contends that the bleeding time may be increased even though the coagulation time is normal and that there may be as much danger from a prolonged bleeding time as from delayed clotting. His method is to puncture the ear and to touch the bleeding point with a piece of filter paper every thirty seconds until the bleeding stops. The normal time is about six minutes.

Widal Reaction.—Agglutination tests of the blood serum against typhoid and paratyphoid bacilli should be made in all cases of splenomegaly in which there is a fever. It must be remembered that agglutinins may be present in the patient's blood as a result of previous prophylactic inoculation with vaccines of these organisms. Under such circumstances, the titer of the serum should be determined and the tests repeated at intervals of two or three days in order to detect possible significant changes.

Wassermann Reaction.—Syphilis is such a frequent cause of splenomegaly and anemia that the greatest care must be exercised in every case, both in the history and in the physical examination, to detect traces of this infection. In addition, a Wassermann reaction should be performed with the blood, and, if necessary, with the spinal fluid. It must be emphasized that a positive Wassermann reaction does not in itself establish a diagnosis of syphilis, and patients may have syphilis in addition to the condition producing anemia and enlargement of the spleen. While it is not subject to absolute proof, it is known that persons have given positive Wassermanns who were presumably free from syphilitic infection or any of the recognized conditions in which positive Wassermanns are recognized as frequent findings. There is also a certain percentage of syphilitics who give a negative Wassermann. *The Wassermann reaction is merely one of the more constant symptoms of syphilis* and should be considered as such in connection with the other symptoms presented by the patient. It has been our experience that the average physician is far too prone to consider a positive Wassermann reaction as pathognomonic of syphilis and thereupon to establish all of the patient's symptoms as the result of that infection. It is for this reason that we wish to urge the greatest caution in the interpretation of the significance of this admittedly nonspecific test.

Icterus Index.—It is often difficult to determine whether anemic patients are jaundiced. A test has recently been introduced by which this question can be answered more definitely than has hitherto been possible. It consists of a comparison, in a colorimeter, of the blood serum with a 1 to 10,000 solution of potassium dichromate. Normally the index is less than six. In a number of conditions it may be somewhat increased, but, if jaundice can be recognized in the mucous membranes, the index will be more than 12. This test has proved to be of much clinical value. In carrying it out, it is necessary to be sure that the patient has not eaten

carrots within twenty-four hours, since they impart a color to the blood serum, and that the standard dichromate solution is made from a pure grade of chemical and is not more than one month old.

Blood Culture.—In all cases in which there is a fever, a blood culture should be made. Ordinarily, aerobic cultures in nutrient broth or agar, or in glucose broth will meet all of the requirements. Occasionally, more elaborate methods will be desirable and should be chosen to suit the individual case. Since the *Streptococcus viridans* may develop very slowly in these cultures, a final report of "sterile" should not be rendered before the expiration of six days' incubation.

Blood Chemistry.—The chemical examination of the blood yields but little information which will aid in the differential diagnosis of the diseases of the spleen. It may, of course, be necessary when it is desirable to determine the functional ability of the kidneys or the presence of diabetes or acidosis. Estimations of urea nitrogen and of creatinin are most frequently used for the former purpose, while in the latter cases the sugar content and the carbon dioxid combining power of the plasma are determined.

Transfusion Tests.—In a certain proportion of the patients who come to the surgeon with diseases involving the spleen, it is desirable or necessary to perform a transfusion with whole blood. It cannot be emphasized too strongly that, in every instance, the compatibility of the bloods of the donor and of the patient should be determined. The dangerous form of incompatibility is that in which the erythrocytes of the donor are agglutinated by the serum of the recipient. Reactions following the transfusion of incompatible blood are often severe and occasionally fatal. The presence of incompatibility may be determined either directly or indirectly.

Of the various *direct* methods which have been proposed, the one of Rous and Turner is the quickest and is very satisfactory. Two 1:10 blood counting pipettes are rinsed with 10 per cent sodium citrate. One is filled with the blood of the patient and the other with that of the proposed donor. Each is emptied into a small test-tube and shaken so as to mix the blood and citrate and thus avoid coagulation. Three capillary pipettes are prepared and filled with mixtures of the two bloods as follows:

Pipettes	Donor's blood	Recipient's blood
1	1 part	9 parts
2	1 part	1 part
3	9 parts	1 part

The contents are mixed by blowing them out upon a slide and drawing them into the pipette several times. The tips of the pipettes are then sealed and allowed to remain at room temperature for fifteen minutes.

At the end of that time, the points of the pipettes are broken, their contents mixed again and a little of the contained blood from each mixed with separate large drops of 0.9 per cent salt solution on slides and covered with cover-slips. The presence of distinct agglutination (not rouleaux formation), as observed with the microscope, indicates incompatibility. If agglutination is present in pipette Number 1, the use of the donor in question is contra-indicated.

The *indirect* method has many advantages. It permits the grouping of numbers of individuals (especially professional donors) so that when an immediate transfusion is necessary, all that has to be done is to determine the blood group to which the patient belongs. A donor is then chosen from that group or, if none be available, from the group of "universal donors." In addition, Karsner has shown that direct matching of bloods may fail to reveal the presence of an incompatibility when the patient is in a very anemic or cachectic condition, for his agglutinins may be too low to become apparent in that method. The indirect method is therefore preferable.

It is unfortunate that there has arisen some confusion in the nomenclature of these groups. Following work by Landsteiner and by Decastello and Sturli, Janský described four groups into which bloods could be divided. Three years later Moss described the same four groups but numbered them somewhat differently. The differences between the two nomenclatures can be seen in the following table:

<i>Janský</i>		<i>Moss</i>
I	(Universal donors)	IV
II		II
III		III
IV	(Rarest group)	I

Both of these classifications have been used and this has led to confusion and misunderstanding in teaching and to the possibility of serious accident in transfusion. The subject has been considered by committees representing the American Association of Immunologists, the Society of American Bacteriologists and the Association of Pathologists and Bacteriologists, who have made the following recommendation: "As further confusion and the possibility of accident may be avoided by the universal use of one classification, it is recommended unanimously on the basis of priority that the Janský classification be adopted." The profession as a whole in this country should therefore adopt the Janský nomenclature.

The method necessitates having on hand a supply of serum from persons of Groups II and III. Blood is drawn under sterile precautions into sterile test-tubes. When the serum has separated, it is mixed with one-tenth its volume of 5 per cent phenol and taken up into capillary pipettes, each of which contains about one drop. These

pipettes are sealed and stored in the ice box where the serum will retain its specific agglutinating power for at least six months and probably longer. One drop each of the II and of the III sera are placed at opposite ends of a glass slide which has been marked for identification. The finger or ear of the person to be grouped is punctured with a needle and two small drops of blood collected at the ends of two glass rods or new toothpicks. These drops are immediately mixed, one with each of the drops of sera on the slide. The cells and serum are mixed by tilting the slide back and forth. In the course of one to three minutes, agglutination, if it is going to take place, will be obvious to the naked eye. The reading may be checked by examining the drops with the microscope, but it is our experience that it is possible to make the reading accurately without that instrument. Reading is made according to the following table, using the Janský nomenclature:

Blood from	Serum II shows	Serum III shows
Group I (Universal donors)....	No agglutination	No agglutination
Group II.....	No agglutination	Agglutination
Group III.....	Agglutination	No agglutination
Group IV.....	Agglutination	Agglutination

It is desirable to select as donor a person who belongs to the same blood group as the patient. Theoretically, persons belonging to Group I may act as donors to patients of any group, but practically, it is found that reactions occur more frequently when this is done. Therefore, Group I donors should be used for other groups only in case of emergency. The donor should be well and strong, have a recently determined negative Wassermann reaction and a hemoglobin of at least 90 per cent.

Examination of the Urine.—There is little to be especially emphasized in the examination of urine from patients suffering with diseases of the spleen. Many, especially the more chronic and the febrile cases, are apt to show a moderate degree of albuminuria and the presence of hyaline and perhaps granular casts. The ordinary routine urinalysis should be carried out and, in addition, care should be taken to examine for the presence of bile pigments and urobilin. For the former we use Rosenbach's modification of the Gmelin test in which the urine is repeatedly filtered through filter paper which is then allowed to dry. This concentrates the bile pigments in the paper so that when a drop of yellow nitric acid is allowed to fall upon it, the play of colors is distinctly seen even though there may be but a very small amount of bile present. We have found the spectroscopic method for the detection of urobilin to be convenient and accurate. To a few c.c. of urine in a spectroscopic cell is added one drop of Gram's iodine solution, which converts any urobilinogen present into urobilin (Conner and Roper). The mixture is then examined with the spectroscope (the small hand spectroscope is

satisfactory) for the presence of the characteristic absorption band located between the Fraunhofer lines E and F, between the blue and the green. In the presence of bilirubin or much urobilin the whole blue end of the spectrum may be blotted out. If this is the case, the specimen is diluted gradually with water and the examinations repeated in order to determine whether at any point it is possible to recognize the absorption band. When there is but little urobilin and much bilirubin, it may be impossible to recognize the former with this method, but such a condition is rarely met with in the diseases of the spleen.

Blood has been found in the urine in cases of abscess of the spleen without real lesion in the kidney. Bence-Jones protein is occasionally found in cases of leukemia (Decastello).

Gastric Contents.—The absence of free hydrochloric acid in the stomach contents is practically constant in pernicious anemia and Stockton has shown that anacidity may be the only symptom which may persist during a remission of this form of anemia. Günzberg's reagent is rather more accurate as an indicator for the detection of free hydrochloric acid than is Topfer's reagent, the one more generally used. Gastric hemorrhage may occur in several forms of anemia and may follow splenectomy.

Duodenal Contents.—Schneider has shown that early and definite information concerning increased hemolysis may be obtained by a study of the contents of the duodenum. Under normal conditions, the duodenal fluids contain bilirubin and occasionally urobilin, but never urobilinogen. In certain pathological conditions, the urobilin is increased and urobilinogen is found in large amounts. For a complete description of the technic of the examination and a discussion of the findings the reader is referred to Schneider's articles.

Feces Examination.—Increase in the amount of urobilin excreted in the stool is recognized to be an index of increase in the amount of hemolysis taking place in the body. The quantitative estimation of this substance in the stool may therefore be of value in making a diagnosis of hemolytic jaundice or in determining the activity of hemolysis in pernicious anemia. Schneider's work would indicate that the examination of the duodenal contents is a more accurate and reliable means to the same end. Certainly it is often difficult to obtain specimens of stool that are fair representatives of the twenty-four-hour excretion, and on that point alone the examination of the duodenal contents is preferable. Occasionally it is difficult or impossible to introduce a tube into the duodenum, and in these cases it is necessary to resort to the examination of the stool. The method used is that devised by Wilbur and Addis and the reader is referred to their article for the full description of the technic. The stool is extracted, the extract treated with Ehrlich's benzaldehyd reagent and examined with the spectroscope. The quantity is expressed in the number of dilutions which can be made before the absorption band of urobilin disappears. In normal persons the

average excretion for the twenty-four hours is about 6,400 dilutions, though the daily variations are quite marked. In pernicious anemia and in hemolytic jaundice, the quantity is much increased, readings as high as 24,000 dilutions having been obtained.

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CHAPTER V

MOVABLE SPLEEN, HERNIA OF THE SPLEEN AND TRAUMATIC LESIONS OF THE SPLEEN

MOVABLE SPLEEN

(Dislocated, wandering, ectopic spleen)

In fetal life the axial mesogastrium becomes adherent to the posterior abdominal wall and the spleen thereafter is relatively fixed in position. It is held primarily by its ligaments, but they do not sustain the full weight of the organ since the tonicity of the muscles of the abdominal wall under normal conditions induces a general intra-abdominal pressure which aids materially in supporting the spleen. The factors, therefore, which might be expected to favor mobility of the organ are: first, persistence of the axial mesogastrium which would render the spleen congenitally mobile; second, acquired conditions which cause undue tension upon the ligaments, namely, increase in size and weight of the spleen, or laxity of the abdominal walls, or both. The relative importance of these factors has been the subject of considerable controversy.

That congenital abnormalities may be a cause of abnormal mobility, either from persistence of the axial mesogastrium or congenital laxity of the ligaments, has been advanced by Ehrich, Toldt and others. In support of this view, Rolleston states that mobility may occur suddenly as a result of a blow in the region of the spleen; also that abnormal mobility occasionally has been met with in several members of the same family. He believes that these features indicate congenital looseness of the ligaments. Moynihan is convinced that a congenital anomaly may exist, since he noted the spleen in a boy of twelve so mobile that it lay in the left iliac fossa. That congenital abnormalities are not a frequent cause is evidenced by the rarity with which mobility of the spleen is noted in children and the infrequency with which defects of the splenic attachments, such as might allow mobility of the organ, are seen in autopsies or dissections upon children. The most striking observation in connection with the etiology of this abnormality is the fact that mobility of the organ occurs almost always in adults, in association with some degree of splenic enlargement which increases its weight. It may be accepted, therefore, that the large majority of cases are of acquired origin; exceptionally, cases may be due to developmental abnormalities.

Apart from the occurrence of movable spleen *per se*, the condition may be associated with general splanchnoptosis. Yet Keith states that in only 2 per cent of cases of visceroptosis is the spleen markedly displaced. In association with visceroptosis, the influences of the splenic mobility, unless torsion occurs, are usually lost in, and cannot be differentiated from, those of the general visceral disturbance. Yet even in such cases, the symptoms due to the spleen may predominate, as in the case reported by Saliba: female, sixty-five years old, weight, eighty pounds, complained of a swelling centrally situated in the lower part of the abdomen, a feeling of heavy weight in the pelvis, severe indigestion, habitual constipation and painful defecation. The symptoms had lasted for many years and she had been conscious of an abdominal mass as long as she could remember. She had had malaria and two pregnancies. On examination, a mass was felt in the midline at the lower part of the abdomen extending upward about three inches from the pubes. The mass was tender, smooth, firm, somewhat triangular in shape, with its base fixed in the pelvis and apparently adherent to the fundus of the uterus. It did not move during respiration. Operation showed it to be the spleen. There was a general visceroptosis. Spleno-pexy was performed.

The large majority of cases of movable spleen are noted in women, and almost always in women who have borne children. The significant feature is the relaxation or atony of the abdominal walls. In some cases, ptosis of other organs is present. In most cases, the mobile organ is pathological, that is, abnormally large and heavy. Enlargements due to malaria have been the type most often noted. But splenomegalies from other causes have been reported. Johnston described a case in which a spleen containing a cyst was found at operation just above the left iliac fossa.

The abnormal mobility usually develops gradually. The ligaments become elongated. The organ descends, taking as a rule a horizontal position with hilum upward. It is supported in the new position chiefly by the gastrosplenic omentum and the splenic vessels, which are elongated. In a recent case we found them fully 5 inches long. The organ often descends directly downward even to the left iliac fossa, or, passing somewhat to the right, may enter the pelvis or reach the right iliac fossa. Adhesions may occur at any point, limiting further descent and further mobility of the organ.

It is said that splenoptosis, in contrast to this progressive course, may develop abruptly. It seems more probable that the condition in such cases has been preëxistent and that attention has suddenly become attracted to the displaced organ.

Chronic congestion of a wandering spleen may occur without torsion of the pedicle. It is stated (Rolleston) that the distended vessels show obliterative changes and thrombosis resulting in fibrotic atrophy of the splenic tissue.

We recently removed a freely movable spleen with long pedicle. Dr. Muller made careful studies of the vessels and found that the blood-vessels of the hilum showed only insignificant changes, namely, slight thickening of the intima. Sections of the spleen presented the appearance of a normal organ. There was no fibrosis and the malpighian corpuscles seemed normal.

The displaced organ draws upon structures with which it is connected or with which it acquires connections and may compress those with which it comes in contact. The stomach is most often affected and may be considerably distorted; the pancreas may be elongated with the splenic pedicle; the intestines and pelvic organs may be affected by pressure and the uterus displaced or even prolapsed.

C. Smith reported an interesting case of "wandering" spleen. He found, on examination, a mass to the right and above the uterus, firm and smooth, and extending as high as the umbilicus. The uterus could be distinctly outlined from the mass, but there seemed to be a close connection between the two structures. During examination, the tumor would suddenly jump to the left iliac region, causing pain. A diagnosis of subserous fibroid was made. At operation, the mass proved to be the spleen attached to the right ovary by a fibrous adhesion. The pedicle measured $1\frac{1}{2}$ inches in diameter extending from the spleen diagonally across the abdominal cavity to the normal splenic region. The spleen was removed.

Zimmermann reports a case of a woman fifty years old, single, virgin, with complete procidentia. Under anesthesia, the prolapse was reduced and a large oblong tumor could be felt lying transversely in the pelvis, not as hard as the uterus yet denser than an ovarian cyst. The abdomen was opened and a large congested spleen was found firmly wedged in the pelvis. The pedicle had three complete turns, which caused congestion but not strangulation of the organ.

Kumaris, in 1915, reported a case of displaced spleen, containing a dermoid cyst, lying in the pelvis. Splenectomy was impracticable on account of adhesions. The first case of movable spleen in a male was reported by Lanz whose patient, a man of twenty-four years, recovered after ligation of the splenic artery.

Torsion of the Pedicle.—If a freely movable spleen does not become fixed by adhesions, rotation upon its pedicle may occur. The immediate cause of such rotation has been attributed both to intestinal peristalsis and traumatism. It also has been suggested, on the basis of Payr's experiments, that rotation may result from extreme blood pressure in the splenic vein. Payr injected the splenic vessels in cadavers and found that the vein elongates and forms a spiral around the artery resulting in gradual rotation of the spleen. There is no other evidence, however, to support this theory.

Torsion may occur suddenly or gradually; the rotation of the pedicle may be of any degree from a partial turn to three or four complete

turns. As the result of torsion, the circulation of the organ is impeded or arrested. If the circulation is only impeded, congestion occurs, which may be followed by hemorrhages into the splenic substance and increase of fibrous tissue and, finally, atrophy. Perisplenitis may also occur with fixation of the organ. If torsion produces arrest of the circulation, engorgement, hemorrhage and gangrene with resultant peritonitis are likely to ensue. Bland Sutton stated, however, that if the torsion is so marked as to obliterate the splenic artery, atrophy of the spleen may occur.

Symptoms.—Mobility or abnormal position of the spleen in itself does not ordinarily distress the patient, but indirectly it may give rise to a great variety of symptoms as the result of pressure or traction upon adjacent structures. These symptoms may be remittent or continuous. Traction on the stomach occurs most often and may cause epigastric pain, nausea and vomiting; compression of the intestines, while rare, may cause obstipation; adhesions between the spleen and the parietal peritoneum may cause pain; pressure on the uterus may cause uterine displacement and affect menstruation. Rectal tenesmus may result from fixation in the pelvis.

In acute torsion, violent symptoms may develop suggesting intestinal obstruction or strangulated ovarian cyst; the spleen itself becomes enlarged and tender. Blackburn and Craig recorded a case of movable spleen with torsion of the pedicle in which the spleen lay in the right lower quadrant and the lesion was mistaken for appendical abscess. Brossmann recently reported a case in which torsion occurred suddenly with violent symptoms. The capsule was ruptured and hemorrhage extreme. Splenectomy resulted in recovery. On the other hand, a slow chronic torsion may occasion no symptoms, or only gradual enlargement of the organ or intermittent pain and tenderness due to perisplenitis.

Diagnosis.—Absence of splenic dullness, the presence of a mass with characteristic notched edge and sharp anterior border, left abdominal position and range of motion upward to the splenic region are factors which render the diagnosis easy in many cases. But these features may not be recognizable. The spleen may be mistaken for movable kidney, ovarian cyst, uterine fibroid, retroperitoneal growths, tumors of the stomach, intestine, omentum or kidney. Such confusion is likely to occur when the spleen is rounded or presents no notch as in a case recently operated upon (*c. f.* Fig. XXVII). When the displaced organ becomes fixed by adhesions in an abnormal position, uncertainty is even more likely to arise than when it is mobile. In all cases of uncertainty, the spleen should be sought in its normal position. But the ordinary diagnostic methods, such as palpation, percussion and X-ray often do not make it clear whether a normally situated spleen is present. Under these conditions, inflation of the peritoneum may be done. This will immediately establish the presence or absence of the spleen in its normal

situation. Suspected lesions of the stomach and intestine can often be excluded or confirmed by means of radioscopic examination. Confusion not infrequently arises as to a movable kidney. It is said that the splenic artery may be felt, but not the renal. It is justifiable to catheterize and inject the pelvis of the kidney for X-ray localization. Enlargements of the kidney may likewise cause confusion. Splenic enlargements develop from above downwards, whereas those of the kidney advance from below upwards. The inflated bowel lies in front of the kidney; whereas the bowel usually lies below or behind the spleen. On bimanual examination, renal enlargements can be felt almost always in the lumbar region, which is not usual in splenic enlargements.



FIG. 27.—MOVABLE SPLEEN REMOVED AT OPERATION.

Spleen $45 \times 8 \times 13$ cm. There are no notches along the anterior edge as the edges are rounded. Microscopical sections present the appearance of a normal spleen.

Treatment.—Mobility or displacement of the spleen which occasions no distress, does not necessarily demand operation, yet the patient should be warned as to the dangers and kept to some extent under observation. Kopp, however, advocates operation in such cases because the mobile spleen may cause disturbance at any time. But the probability of untoward developments, such as torsion, is not so great as to indicate operation in all cases of mobility or displacement. If symptoms develop referable to the spleen, operation is advisable. If torsion occurs, operation is imperative.

The operative procedures which come into consideration are splenectomy and splenopexy with intraperitoneal or retroperitoneal fixation of the spleen. Although the immediate results of splenopexy are claimed to be favorable, the late results are uncertain. Splenectomy is, in general, the better procedure, in view of the fact that the spleen is usually pathological, the operation is easy by reason of the elongated

pedicle and by this operation only can recurrence unquestionably be prevented.

W. J. Mayo (1913) reported three wandering spleens, two treated by splenectomy and one by splenopexy by suture and packing with gauze. In this case the spleen remained in place but the patient suffered more or less pain. He regards splenectomy as the wiser plan.

Some believe that the congested spleen, once replaced, will become reduced to normal size, but Hall observed nothing suggestive of this in his eight cases. Yet in the case of Blackburn and Craig, thirteen months after the spleen had been replaced in its normal position it had apparently diminished one half. Moynihan quotes the following results: Kowers' first case, fixed by tamponade, was well four years after operation with spleen fixed in good position. In his second case, the spleen had dropped a little, but its mobility was considerably lessened by the operation.

Rydygier's patient was seen fourteen months after the operation and the condition was satisfactory. The spleen had been placed in a peritoneal pocket.

Greifenhagen's patient was seen seven months after operation and the spleen was in good position and securely fixed. The spleen had been anchored by sutures to the abdominal wall.

Technical details of the various operations for fixation of a movable spleen are given in the chapter on operative procedures.

The mortality of splenectomy for movable spleen has been comparatively high. This is said to be due to serious changes of the vessels in the pedicle of the spleen. Sudden death resulting from thrombosis of the pulmonary artery, several days after operation, came under Finkelstein's notice in 2 cases. Salis reported a similar experience.

Johnston, in 1908, collected 100 splenectomies in cases of movable spleen with 7 deaths. Finkelstein reported an even higher mortality. Of 39 cases with twisted pedicle, collected by Johnston, 10 died.

The statistics of Johnston and Finkelstein indicate a relatively high mortality following splenectomy for movable spleen without torsion. Yet beneficial results should be confidently expected in properly selected cases and there should be little operative risk. With torsion, the prognosis should in general be good, provided there is prompt recognition that a surgical condition exists.

HERNIA OF THE SPLEEN

The spleen may be found as part of the contents of a diaphragmatic hernia. Rochard found that in 300 cases of diaphragmatic hernia, 78 involved the spleen. In a recent autopsy case which came under our observation, a young girl presented in the left dome of the diaphragm an opening about three inches in diameter through which intestines and spleen had passed into the thorax. Heitzmann described a unique case

in which a spleen was found in a left-sided indirect inguinal hernia. At operation, the vaginal process of the peritoneum was found to contain a purplish strand the thickness of a finger, which tapered off toward the abdominal cavity, passing up towards the region of the real hilum where it was attached. The strand was detached about 12 cm. from its insertion and was microscopically found to contain pure splenic tissue.

TRAUMATIC LESIONS *

It is generally stated that the spleen is involved in about 20 to 23 per cent of all traumatic lesions of the parenchymatous abdominal viscera. But it is probably injured much more frequently than the published observations indicate, since a considerable proportion of the cases do not come under clinical observation. This is especially true in severe injuries, for many of these patients succumb a short time after the injury as a result of the profuse hemorrhage which is the inevitable result of grave traumatism to this organ. Traumatic lesions comprise subcutaneous injuries and open wounds. Under subcutaneous injuries will be considered spontaneous as well as traumatic ruptures.

Subcutaneous Injuries (Contusion, Rupture).—Subcutaneous injuries are much more common than open wounds; Michelson's statistics (1913) comprise 298 cases as compared with 82 gunshot wounds and 52 stab or incised wounds of the organ.

Though subcutaneous injuries of the spleen have occurred at all ages, they are most common in men during the active period of life. Since a normal spleen is relatively small and is fixed in a protected position, wounds of such an organ are unusual except as the result of extreme violence. On the other hand, diseased spleens are often large and friable and reach below the costal arch, thus lying in an exposed position. Consequently this type is far more frequently injured; moreover rupture of such diseased organs may occur as the result of comparatively slight violence. Malaria is the most frequent cause of such an enlargement. The malarial spleen is not only more exposed to traumatism on account of its position, but its diminished elasticity and secondary capsular changes favor serious destructive lesions of the organ. Berger collected 132 cases of rupture of a diseased spleen, among which 93 were malarial. Rupture of the organ has been noted in the newborn by Steffen (2 cases) and by Charcot. The enlarged spleens in these cases were probably due to syphilis. Rupture has also been reported following trauma in Banti's disease (Blecher) and in other types of splenomegaly.

Spontaneous ruptures occasionally occur in diseased spleens such as the large friable spleen of typhoid. Spontaneous rupture will be considered at some length in a subsequent paragraph.

* "Injuries to the Spleen," Boston Medical and Surgical Journal, March 1, 1923, p. 262. Read before the New England Surgical Society, September 23, 1922.

A subcutaneous injury of the spleen may be caused by direct or indirect violence. Injury to the organ by direct violence may be brought about in various ways, such as a kick by man or animal (Walker) or a fall from a height (Ballance, Latouche), the force being exerted immediately over the organ; or the lesion may occur as a result of compression, as when the body is run over by a wheel. In these cases, the spleen is usually crushed or burst. But the lesion may also be caused by a fractured rib driven into and tearing the organ. In indirect violence the force is exerted at a distance, as a fall upon the buttocks, feet, knees, kick by a horse in the sacral region, or fall upon a remote part of the trunk. Muscular violence has apparently been the cause in rare cases, the injury following vomiting (Kernig), sneezing (Roeser), or childbirth (Simpson). But in such cases the spleen must have been extremely friable. Stone reports 2 cases which he attributed to muscular violence:

1. Indian woman, age thirty, while carrying a large vessel of water on her head made a sudden movement to save vessel from slipping, immediately fell down and died soon afterwards. Autopsy showed three superficial tears in the spleen. The organ was very large and soft. There was no ecchymosis of the muscles over the organ. Stone lays particular stress on this point with regard to the medicolegal aspect.

2. Indian woman of thirty-seven who was struck in the face by her husband. She attempted to avoid him, fell and died soon afterwards. Examination fifteen hours after death showed a long perpendicular rent in the spleen. The organ was diseased, was of the consistence of thick cream, had a very delicate capsule and weighed in its empty condition $1\frac{1}{2}$ pounds.

Pathological Changes in Subcutaneous Injuries.—Any part of the spleen may be affected. The lower extremity of the organ, being the least protected, is especially exposed to traumatism acting from below the ribs; whereas a force which produces one or more fractures of the lower ribs will cause an injury higher in the spleen. Associated lesions of the abdominal organs are rare. The left kidney has been ruptured coincidentally in some cases (Gardiner, Hughes), the frequency of this lesion being placed as high as 12 per cent. The colon, liver and pancreas have seldom been injured. In rare cases the lung has been injured.

Subcutaneous injuries may be divided into injuries without rupture of the capsule (contusions) and those with rupture of the capsule (ruptures).

Contusions consist of intracapsular lacerations of the parenchyma. The intrasplenic hemorrhage is variable in degree but may be considerable. The splenic lesion may heal rapidly and the blood, especially if small in amount, may be absorbed and leave little or no evidence of the injury. On the other hand, abscesses not infrequently develop as

the result of hematogenous infection. Large uninfected accumulations of blood may leave cicatricial areas of considerable size, veritable fibrous tumors, or they may become encapsulated and form cysts (Terrier, Heurtaux, Camus).

Where the injury involves the capsule, constituting a rupture of the organ, the lesions may vary from slight rents of the parenchyma and capsule to extensive destruction of the splenic tissue. The fissures may be clean-cut or lacerated, single or multiple. Fragments of variable size may be completely separated. The whole spleen may be separated at its hilum. Occasionally, the vessels only have been torn and, in a case reported by Pohl, the vein was divided and the artery intact. The patient in this case was a child three and one half years old, who was run over by the wheels of a wagon.

Hemorrhage regularly occurs and may be extreme. Blood often accumulates as a coagulum near the spleen (Camus, Plucker), as a result of clotting and adhesions, but free bleeding into the great cavity is frequent.

Hemorrhage is occasionally delayed for a considerable period after the injury. Several explanations have been offered. Neck attributes the delayed hemorrhage to the insertion of bloody coagula in the splenic ruptures, the hemorrhage being thus suppressed by "tamponade." Demoulin believes it is in some cases due to a large sub-capsular hemorrhage which ultimately bursts the detached capsule.

Nast-Kolb, as the explanation in his case, assumes that the omentum "packed" the splenic wound immediately after the injury. This sufficed for the suppression of the hemorrhage until the agglutinations ruptured and blood was poured into the abdominal cavity.

Wounds of the spleen if small may undergo repair. The surface becomes covered by a clot which organizes in a short time. The omentum not infrequently becomes adherent to the clot and reinforces the scar (Gourrin). The repair of these wounds has been studied by Mayer in animals.

A localized perisplenic hematoma may be absorbed, may become encysted or may be infected, causing an abscess (Bonnamour and Bouchut).

The *symptoms* of contusion and rupture of the spleen are extremely variable, depending upon the extent of the lesion, the character of the traumatism, and especially the previous condition of the organ (hypertrophy; adhesions). The mildest and severest types are apt to escape detection, the former passing as simple regional contusions or costal fractures, while extensive ruptures are always associated with profuse hemorrhage and are often promptly followed by death. The symptoms in the intermediate group are divided into those due to traumatic shock, internal hemorrhage and abdominal manifestations.

In contusions there may be pain, tenderness, local muscular rigidity and increase in the size of the spleen. The spleen may gradually increase

to a marked degree. Heurtaux reports a case containing ten liters within the unruptured capsule. In some cases there is intermittent fever. Rupture of the capsule may occur at any time with internal hemorrhage and its symptoms, or suppuration may develop with the symptoms of abscess. The pain in all injuries of the spleen is often referred to the left shoulder and may be ascribed only to this region. Yet Connors in a considerable experience never noted this feature.

Rupture of the spleen gives rise to the symptoms of hemorrhage and shock. The degree varies widely and is dependent upon various factors. Shock may be extreme and result fatally within a short time, but hemorrhage is usually the important factor. Berger states that 51.8 per cent of cases of rupture of the spleen die within one hour as the result of hemorrhage.

In the early period after the injury it often cannot be determined whether the symptoms are due to shock or internal hemorrhage. The initial picture of shock may be prolonged indefinitely as the result of hemorrhage. In an extensive lesion, the one follows and fuses with the other, and there is often no means of differentiating the symptoms of the two. Not infrequently, however, there is a latent period between the subsidence of the shock and the development of clinical manifestations of internal hemorrhage. Thus, in one of d'Auvray's cases, the symptoms of hemorrhage did not develop for eighteen hours. It is unnecessary here to enter into the general clinical manifestations of shock and hemorrhage.

Some indication of accumulation of blood within the peritoneal cavity may often be obtained by percussion. The flanks, especially the left, present undue dullness if blood accumulates to a marked degree. Some writers, especially Pitts and Ballance, and Chavannaz, attach much importance to the following peculiarity which they believe is frequent. Percussion over the right flank with patient turned on left side gives tympanitic note; whereas the reverse, percussion over left flank with patient turned on right side, continues to give dullness by reason of clots. This has been termed the sign of Ballance. The blood changes are often suggestive, in that hemorrhage gives an early and rapid rise of leukocytes, not accompanied by a relative fall in hemoglobin and red cells. Thus, in a boy of ten, who was run over and whose spleen was ruptured and subsequently successfully removed, about half hour after accident the blood showed:

W. B. C. 34,400	Polys. 77 per cent	Hgb. 93 per cent
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Two hours later:

W. B. C. 45,700	Polys. 88 per cent	Hgb. 93 per cent
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But it must be recognized that a considerable increase in leukocytes takes place in shock according to Brodin and Saint Girons.

Reference must be made to those cases in which symptoms of internal hemorrhage develop a considerable period after the injury, the individual having been free from all symptoms during the interval. The condition is well illustrated by a case of Nast-Kolb. The patient was a robust man, who, after the kick of a horse in the splenic region, felt quite well for four days, except for slight pressure pain in the left side of the chest. The observer especially emphasized the fact that the temperature did not rise during the entire course, although several writers have called attention to elevation of temperature in splenic injuries as an important diagnostic aid. Left-sided shoulder pain, a sign which is somewhat characteristic of splenic injury as emphasized by Levy and others, was likewise absent. Without prodromata and while in good health, the catastrophe overtook the patient when danger seemed to have passed. While straining on a bed-pan he suddenly collapsed and presented the condition of profound shock. This became steadily worse, with progressive anemia. Dullness was demonstrable in the splenic region. The diagnosis of splenic hemorrhage was made and immediate operation undertaken. The abdomen contained a quantity of fluid blood. A large rupture could be felt on the convexity of the spleen. The organ was entirely encased in loose omentum which was detached without difficulty. The splenic pedicle was ligated and the spleen removed. In its upper third was a tear 5 cm. in length, passing through almost the entire thickness of the organ. There was another tear in the lower half, 6 cm. in length.

Hahn reported an impressive case in which, seven days after the infliction of indirect violence, fatal hemorrhage occurred from a subcutaneous rupture of the spleen, which up to that time had caused no symptoms. Extirpation of the spleen failed to save the patient's life. The cavity contained a large amount of fluid blood. There was a tear on the posterior wall of the spleen and a blood-clot larger than a fist lay behind the organ. The patient, a coachman, had been flung to the sidewalk, striking his right side. It is probable that the splenic wound became closed through the pressure of the primary blood-clot. On the fifth day after the accident, the patient took a short journey by rail, which probably induced the profuse secondary hemorrhage.

In a review of the cases of delayed hemorrhage of the spleen reported in the literature, Nast-Kolb states that the time that elapsed between the injury and the operation varied between one and a half and nine days. The lesions were always very extensive lacerations of the organ. Of the 9 cases which were operated upon, 3 died. The author emphasizes the fact that no new guides for diagnosis could be obtained from the reported cases; and that a suspicion of a splenic injury should arise in all severe traumatism to the left side of the chest or abdomen, and such patients should be closely watched for a considerable time. At the first evidence of internal hemorrhage operation should be undertaken.

Prognosis.—Death may occur rapidly or after an interval of a few hours from shock and hemorrhage, or the blood may clot for a time and hemorrhage be temporarily arrested or retarded and death from hemorrhage be delayed for several days.

The prognosis is unqualifiedly bad in rupture of the spleen in cases that are treated conservatively. The mortality is given by Berger as 84 per cent and by Choux as about 96 per cent. Berger estimates that 51.8 per cent die in the first hour. He states that 90 per cent of deaths are due to hemorrhage and 10 per cent to infection. In contrast to the appalling outlook without operation, surgical treatment has given much more favorable results. Thus, Chavannaz has compared the statistical tables from 1897 to 1909 and finds steady improvement on account of earlier diagnosis and better surgery. The mortality of splenectomy was as follows:

MORTALITY TABLE (1897-1909)

Year	Statistics	Per 100
1897	Vanverts	55.5
1901	Fevrier	50.
1902	Eisendrath	44.
1902	Berger	41.
1908	George Ben Johnson	34.
1908	Finkelstein	39.5
1909	Plason	37.

Nephrectomy and splenectomy have been performed successfully for injuries to both organs (Caplesco). Savor, 1918, reported a case of a woman, six months pregnant, in whom splenectomy was performed successfully as regards mother and child. Johnston collected one hundred and fifty splenectomies for trauma of spleen with a mortality of 34 per cent. Willis reported in 1919, 4 cases of subcutaneous traumatic rupture of the normal spleen for which splenectomy was performed, with 3 recoveries and 1 death.

Treatment.—Splenectomy is the operation of choice and should, in general, be employed; yet adhesions may occasionally render splenectomy impossible in view of the condition of the patient. In such cases, suture or tamponade may be attempted for small tears. In a large wound, clamps or ligatures may be placed on the pedicle to control bleeding and the operation subsequently completed after reaction of the patient has occurred. Suture (splenorrhaphy) is not a reliable procedure, because the stitches often tear through the friable spleen and render the condition worse. However, it has proved successful in some instances. Berger cites 2 cases of splenorrhaphy for rupture of spleen with 1 recovery. Tamponade is likewise unreliable; yet Berger collected 6 cases of tamponade for rupture with 1 death and believes it is

applicable for small tears complicated by marked adhesions and bad condition of patient.

It has been shown by the investigations of Carrière and Vanverts that ligation of the pedicle causes necrosis of the organ and, therefore, is not advisable. Ligation of the artery alone is said to cause atrophy of the parenchyma. It is possible, therefore, that this might be justifiable in conjunction with tamponade if very firm adhesions are encountered. Yet Cejudo has recently reported necrosis and suppuration of the spleen after ligation of the artery in a case of Banti's disease.

Since diagnosis is often doubtful, the operation must be planned for a complete exploration. This must, however, be rapid and associated injuries must be thought of and sought. The technical details of splenectomy are given in the chapter on surgical procedures.

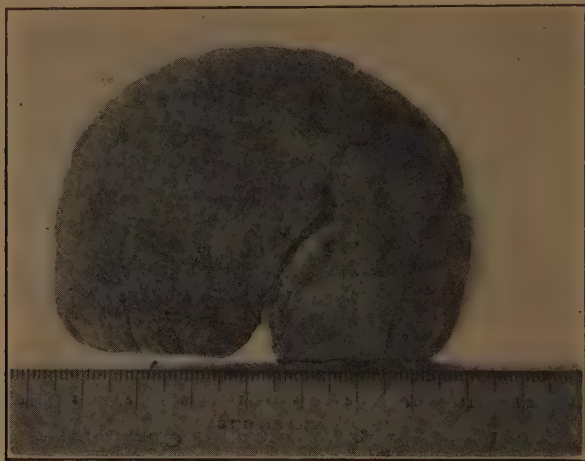


FIG. 28.—RUPTURE OF SPLEEN.
Successfully removed at operation.

The following illustrative case is of interest. A boy of ten years was admitted to the New York Hospital on May 22, 1920, complaining of pain in the abdomen. About ten minutes before admission, he had been thrown down by a touring car and one wheel had passed over the upper abdomen in the region of the costal arch. When first seen, patient appeared to be in moderate shock. Face and lips were pale; breathing was rapid and accompanied by an expiratory grunt; pulse 96 and of fair quality. Temp. 98, resp. 32. The hands were cold and clammy. The boy did not complain of thirst or air hunger, but he was restless, complained of severe pain in abdomen and gave evidence of shock; the face was pale and covered with sweat; expression anxious. Breathing was almost entirely costal in type. There was no evidence of fractured ribs. The lungs were clear. Fluoroscopic examination of chest was negative.

Abdomen was rigid all over, but especially in the upper half. There

was marked tenderness in epigastrium and right upper quadrant; slight generalized abdominal tenderness. Abdomen not distended nor yet scaphoid. Dullness in both flanks, no fluid wave. No obliteration of liver dullness. No shifting dullness. For blood count see p. 93.

Patient showed clinical evidence of internal hemorrhage. Pulse became more rapid and weaker. He complained of thirst and showed evidence of air hunger. Abdominal signs showed little change aside from increase in area of dullness in flanks.

Laparotomy revealed a badly lacerated spleen bleeding actively, with about 700 c.c. of blood in the peritoneal cavity. No other lesion. Splenectomy was done (Dr. S. Erdman). Infusion was given on operating table. Patient made an uninterrupted recovery.

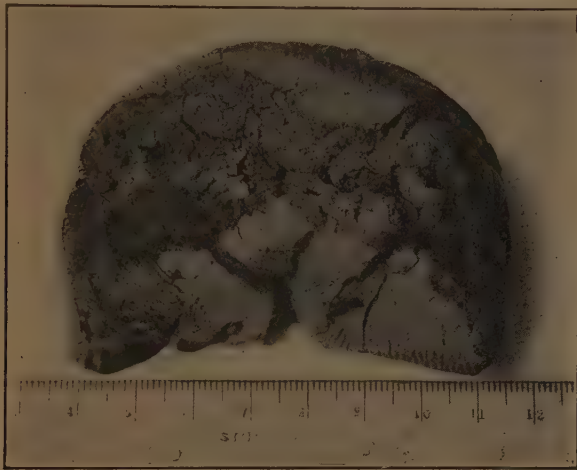


FIG. 29.—RUPTURE OF SPLEEN.
Same case as preceding picture.

As a substitute for transfusion in cases of traumatic rupture, Hauke collects the blood from the abdominal cavity, mixes it with 0.5 per cent sodium citrate solution and injects it intravenously. This procedure should not be elected in preference to transfusion when a suitable donor is available and facilities for transfusion are at hand; it is, however, of value when a transfusion cannot be given.

Spontaneous rupture may occur in diseased spleens without apparent trauma. Cimbali (cited by Litten) mentions the case of a man sixty-five years of age whose spleen was much enlarged as the result of malaria; though apparently in normal health, on rising from bed rupture of spleen occurred. This was demonstrated at operation, which was not successful. Noland and Watson, Leighton and others have also reported rupture of malarial spleens. Leighton presents abstracts of the reported cases. Spontaneous rupture also has been noted in typhoid, puerperal infection, labor (Hubbard), pregnancy (Schwing, Simpson), relapsing fever, typhus and tuberculosis (McCoy). The complication is of the greatest importance in typhoid, and this sequel

to the disease demands some elaboration. Conner and Downes described a case and reviewed the reported cases of spontaneous rupture of the spleen in typhoid fever. They state that only 12 other cases are recorded in the literature. These were collected by Melchior, who added an additional case, which Conner and Downes exclude. In 9 cases, the condition was discovered at autopsy. In 3, it was found in the course of operation for supposed intestinal perforation. None of these cases recovered. The infrequency of the complication is shown by the statistics of Curschmann. In 577 autopsies on typhoid patients, only 2 cases of rupture of the spleen were found. All of the 12 cases recorded by Melchior were males, 10 adults and 2 boys of eight and ten years. The time of rupture in the 13 cases (12 collected by Melchior, and 1 described by Conner and Downes) occurred as follows:

- 5 cases second week.
- 2 cases third week.
- 1 case fifth week.
- 1 during convalescence.
- 3 no record.
- 1 during an apparent relapse.

The rupture apparently may involve any part of the surface, is usually linear and may be limited to the capsule or reach deeply into the parenchyma. The depth apparently does not determine the degree of hemorrhage. The symptoms in the recorded cases lasted from a few hours to three days. The symptoms of rupture of the spleen, Conner and Downes state, fall into two distinct groups: (1) the local symptoms of the rupture and of irritation of the neighboring peritoneum by the extravasated blood; and (2) the general symptoms of severe internal hemorrhage. In most of the cases described, pain seems to have been the first symptom, although the location and character of the pain have usually not been given in much detail. A picture of the condition can best be given by a summary of their case.* The patient, a male, age thirty-six years, was admitted to the New York Hospital on February 20, 1913, with the diagnosis of typhoid fever. His symptoms had begun seven days previously.

On February 21, he complained of a sudden sharp, stabbing pain in the left hypochondrium. This was followed by severe aching pain in the left shoulder, which radiated somewhat down the left arm. Soon after the onset of the pain, he vomited a small quantity of clear fluid and broke into a profuse perspiration. The respirations were rapid and shallow; there was marked tenderness to pressure just below the costal margin, where the spleen could be distinctly felt, and slight rigidity of the upper part of the left rectus muscle. February 22, patient looked very seriously ill. His eyes were sunken, his features drawn and anxious, his respirations shallow and hurried. February 24, patient's condition was improving.

On the morning of February 25, he had a similar attack with the sunken eyes, the pinched features and anxious look that had characterized his first attack. His pulse was rapid, small and soft; his respirations also were rapid, the skin was covered with cold sweat and he complained of weakness and nausea. There was dullness on percussion over the greater part of the left side of the abdomen and in the left flank, and some rigidity and tenderness in the left upper quadrant. The symptoms pointed strongly to an alarming loss of blood, but the blood examination seemed inconsistent with this conclusion. Red cells, 5,280,000; hemoglobin (Sahli), 85 per cent; leukocytes, 35,000.

On operation by Downes, the abdomen was found to contain a large amount of blood, estimated at from one and a half to two quarts. "When the hand was passed behind the spleen, a rent in the capsule, fully three inches in length, was encountered running along the posterior border, and during the manipulation this rent was so enlarged by the time the organ was brought out of the wound that the capsule had been stripped from almost half its surface." The spleen was removed and the patient made a comparatively uneventful recovery.

The authors state that the discovery at operation of a layer of old, laminated clot lying directly over the dorsum of the spleen made it certain that the acute symptoms which appeared three days before the operation indicated the time of the first rupture of the splenic capsule. These symptoms had entirely subsided before the second attack of coughing. At this time evidently there was either an increase in the rupture of the capsule or a displacement of the old clot and subsequent uncontrollable bleeding from the site of the tear.

A second point of interest, they state, relates to the character of the blood examination at a time when all the symptoms indicated an alarming internal hemorrhage. The case illustrates that increase in the leukocytes occurs much earlier than do the other characteristic blood changes, namely, the fall in the number of red cells and in the percentage of hemoglobin.

The *treatment* of the condition is obviously surgical; and the severity of the hemorrhage is often so great that early operation is essential. The possibility of the complication, therefore, should be held in mind and suggestive symptoms should decide one in favor of immediate operation. Preparations should be made for giving a transfusion as soon as hemorrhage is checked; or, if the condition is extreme, transfusion and operation may be begun simultaneously. Under local anesthesia, an exploratory incision was made by Downes in his case and general anesthesia was administered when the diagnosis was verified. This is probably the best routine to follow. In the absence of facilities for transfusion, a saline infusion should be substituted.

Open Wounds of the Spleen.—By reason of the small size and protected position of the spleen, open wounds of this organ are relatively rare both in civil practice and in modern warfare.

In civil practice such wounds are most commonly produced by bullets, the greater frequency of gunshot wounds as compared with stab and incised wounds being accounted for by the anatomical position of the organ.

In stab wounds, which are usually inflicted from above, the wound is often in the lower left thorax, consequently the pleura, lung and diaphragm are frequently involved. But the wound may involve the left hypogastric or lumbar regions. In gunshot wounds, the bullet enters the abdomen more often than the thorax. Therefore, injuries of the gastro-intestinal tract and kidney predominate as associated lesions. The wound of entrance may be at a considerable distance, as the epigastrium, right hypochondrium, right thorax or even more remote sites. The degree of injury to the spleen varies. A narrow blade such as a stiletto may cause only a small wound. A bullet at the height of its course, unless deflected by bony structures, penetrates like a stiletto, with no explosive effect. Under such conditions the splenic wound may be small and the wounds of entrance and exit in the abdominal or thoracic walls are punctate. On the other hand, a bullet at the beginning of its course or when almost spent will produce irregular and lacerated wounds in the spleen and the overlying soft parts.

War Wounds of the Spleen.—The experiences gained in the recent War are worthy of analysis. While relatively infrequent, in the aggregate they comprise a considerable number of cases. Certain deductions may be drawn which apply somewhat to wounds in civil life.

Frequency of Occurrence.—The 1920 report shows that for our troops in France there were 49 battle wounds involving the spleen, of which 31 resulted in death. The tabulations of operations are not complete, but the records do show that of 10 splenectomies, 8 died (General Ireland, personal communication).

From the British forces, Wallace reported that in 965 abdominal operations, the spleen was found wounded 54 times. In 32 instances it was the only organ damaged.

In modern warfare, open wounds of the spleen result especially from fragments of high explosive shells, but also from rifle or machine-gun bullets, rarely from sharp weapons. The wound of entrance most often is in the lower left thorax, left hypochondrium or lumbar region, but it may be at a considerable distance, entering the epigastrium, right hypochondrium, right thorax or even more remote situations. In addition to the direct wounds of the spleen, rupture of the organ may occur indirectly, especially by large fragments of projectiles which have not actually come into contact with the organ. Such injuries are more likely to occur in a pathologically enlarged spleen which is abnormally friable.

Wallace reported 2 cases of ruptured spleen produced by shell fragments which did not themselves touch the organ. The left lower chest was hit and the ribs broken. In one the diaphragm was intact. In the

other the diaphragm was ruptured over a small area and there was a corresponding wound on the outer surface of the spleen with radiating fissures showing that the spleen had been burst by an indirect blow.

Bullet wounds with punctate entrance and exit do not differ materially from similar wounds in civil life, but lacerated wounds, whether caused by bullets or sharp weapons, must be considered as having more or less the characteristics of wounds caused by shell fragments. The essential difference from wounds of civil life is the greater destruction of tissues and the far greater probability of the introduction of pyogenic and gas bacillus infection. In the case of high explosive shells, the irregular fragments carry into the tissues bits of clothing laden with organisms and deposit these along the tract, the walls of which are devitalized by the rough fragments. Such devitalized tissue acts as an admirable medium for the growth of pathogenic microorganisms.

Pathological Anatomy.—All degrees of injury to the organ may occur; penetrating, gutter, perforating, lacerated wounds, or ruptures with separation of a segment. The friability of the tissue is so marked that extreme destruction and large tears are the rule, yet limited, clean-cut wounds occasionally occur. In the majority of cases of wounds by shell fragments, deep irregular fissures radiate from the orifices of entrance and exit, at times completely separating segments of the organ. Moreover, in most cases, as a result of contusion, a large part of the parenchyma is converted into an almost fluid pulp (Fiolle).

The splenic pulp when wounded is prone to give rise to hemorrhage of extreme degree, so much so that a large proportion of cases in warfare do not survive transportation from the battlefield to a hospital where surgical measures may be undertaken for the arrest of the hemorrhage. This is notably the case in wounds involving the pedicle of the organ. The splenic pulp is, moreover, peculiarly prone to infection. Consequently the late development of an abscess within the organ and subphrenic abscess is not uncommon.

Associated Lesions.—Of the thoracic organs, the *pleura* is most frequently coincidentally wounded; the lung not infrequently; the pericardium rarely (Stern). Stern's patient presented a large wound at the left base of the thorax, through which protruded the ragged lower pole of the herniated spleen. The organ was reduced to a bloody mass, the diaphragm was torn and there was a rupture of the pericardium. Splenectomy was performed, but the patient died.

With wounds of the pleura and diaphragm, hemothorax may result. If the diaphragmatic opening is large, the blood may flow into the pleura rather than into the abdomen. In one case, hemopericardium developed (Hallopeau).

Of complicating injuries of abdominal viscera in war wounds of the spleen, according to Fiolle, wounds of the small intestine have most frequently been reported; after which, in order of frequency, lesions of the colon, the left kidney and the stomach are seen as associated

injuries, the pancreas and the liver being much more rarely wounded. Wallace, on the other hand, found the kidney the most frequently involved. Subsequent peritonitis is common, even when the spleen alone is injured.

The thoracic and abdominal walls are sometimes so widely opened as to permit hernia of the spleen. This is far more likely to occur with a posterior than with an anterior wound.

Delore and Kocher state that the prognosis of thoraco-abdominal wounds, with isolated injuries of the spleen, is essentially governed by the presence of pleural rather than peritoneal complications. Fiolle states that like all war wounds, those of the spleen are very easily infected, but as the organ is relatively isolated from the great serous cavity by its situation and by the barrier of the stomach and the colon, the infection tends to become localized and subphrenic abscesses are common. The course of such abscesses is peculiarly rapid and malignant, the patient usually succumbing within a few days under severe general symptoms. When the diaphragm has been perforated, these abscesses may break into the thorax, giving rise to purulent pleurisy.

Symptoms and Diagnosis.—As has been emphasized, the high subdiaphragmatic position of the spleen exposes it rather more to wounds involving the thorax than those exclusively confined to the abdomen, and, for this reason, splenic complications are frequently overlooked.

There is no way of determining the fact that the spleen has been wounded. This is largely due to the usual occurrence of associated lesions which mask the picture, for instance, an open wound of the thorax, a perforating wound of the intestine or a wound of the kidney. Even when the spleen is the only organ wounded, there are no symptoms which call attention to it. Internal hemorrhage may arise from various sources. Moreover, internal hemorrhage of considerable degree from the spleen or elsewhere may occur without recognizable symptoms for a considerable time in view of the associated marked degree of shock which usually attends such wounds. Of course, if severe hemorrhage is noted from the external wound, there can be no question of a serious lesion; but even then its source is doubtful.

The diagnosis of stab and gunshot wounds of the spleen offers especial difficulties in view of the absence of a definite symptomatology and the frequency of associated wounds of other organs. The direction of the wound, the evidence of internal hemorrhage, pain and muscular rigidity in the left hypochondrium may lead to a presumptive diagnosis that the spleen has been wounded; but conclusive evidence is rare.

Radioscopic examination sometimes aids in the diagnosis. The shadow of the spleen may be visible on the screen and a shell fragment or bullet can sometimes be localized in the organ. A foreign body was localized on the hilum of the spleen in one of Fiolle's cases.

The mortality has been given as 60 per cent (Mayer) and 53.8 per cent (Edlers). Lebreton reported 17 cures in 28 cases of gunshot

wounds. Wallace found the mortality 50 per cent in uncomplicated and 63.6 per cent in complicated cases. The prognosis depends upon many factors, including the size and situation of the wound, previous condition of the organ (fibrosis tends to limit the hemorrhage) and associated lesions.

The prognosis is serious even in relatively slight wounds in which hemorrhage is temporarily stopped, because it is likely to recur and then may be excessive and even fatal. Permanent arrest of the hemorrhage by operation is, therefore, strongly indicated.

Treatment.—The treatment of open as well as subcutaneous injuries of the spleen is exclusively surgical. If there is merely a suspicion of internal hemorrhage, operation is indicated. Prior to operation, quiet should be enforced and morphin administered. Transportation should be as gentle and expeditious as possible, and all methods should be observed for combating shock. But transfusion in general should be delayed until after the patient is on the table and hemorrhage is either arrested or is to be arrested immediately by operative procedures.

Since the course of the projectile cannot be determined accurately before operation, the incision or incisions must usually be so planned as to allow adequate exploration and, in lacerated wounds, excision (*débridement*) of contaminated tissues of the abdominal or thoracic walls. This is often done through a separate incision.

The incision must depend upon the site of wound and regions to be explored. The operator must be prepared to explore a wide area of the peritoneal cavity, and for this purpose a median incision may be elected. This can be modified if necessary for splenectomy after the cause of the bleeding has been identified as splenic. For stab wounds or bullet wounds evidently confined to the splenic region, the incision may be planned for immediate exposure of the spleen. In some cases, the course of the tract must be followed for exploration, in which case the tissues along the tract should be excised.

If the wound is in the hypochondrium, a transverse incision or oblique incision along the costal arch may be employed with excision of the wound of entrance. In thoracic wounds it is best to follow the tract through the thorax and to establish the fact that the abdomen has been penetrated. The diaphragm and thoracic wound are then repaired and an independent abdominal incision made for exploration and exposure of the spleen. In some cases, however, if there is evidence that the projectile has not penetrated far beneath the diaphragm, the wound in it may be enlarged and exploration of the spleen made through it. It has been recommended that when thoracotomy has revealed penetration of the diaphragm and the spleen, wider exposure be obtained by an incision downward from the wound sectioning the ribs and extending downward along the outer border of rectus, the diaphragm also being sectioned from the wound to its insertion, thus making with retraction

a wide exposure. An independent abdominal incision, however, appears preferable.

After the spleen has been explored and found to be wounded, splenectomy is in general the proper procedure, since it may be quickly performed, meets the indications of permanently controlling hemorrhage and is apparently harmless from the standpoint of subsequent health. When the spleen is so firmly adherent as to render its removal dangerous, other methods of an emergency nature may be employed. Small linear tears have been closed by suture with fine round curved needle. The suture of a piece of free omentum in the wound is a valuable measure to aid in the control of hemorrhage. However, the friability of the organ renders control of hemorrhage by suture uncertain. Packing is regarded by Wallace and Fiolle as preferable. The gauze should be left *in situ* about ten days (Fiolle). As a last resort, clamps may be left on the pedicle and splenectomy performed after reaction from shock.

Prolapse of the Spleen (Traumatic Hernia).—The spleen may pass, as a whole or in part, through a wound in the abdominal wall or lower left thoracic wall, especially in those cases where a long splenic pedicle exists. The extrusion of the organ, as stated by Moynihan, is due to the fact that in the acme of his sudden agony the patient strains heavily and compresses the chest and the abdominal walls. The condition is infrequent. It is noteworthy that a part of the organ or the entire spleen may prolapse through a relatively small wound or even through an intercostal space. As a result of constriction of the organ by the margins of the wound, the prolapsed spleen often undergoes considerable increase in volume and degenerative tissue changes which may result in gangrene.

The *symptoms* are often very slight. Pain is usually not severe, the spleen being an insensitive organ, and hemorrhage is often not active, because the organ becomes tightly compressed between the lips of the wound and the circulation is interrupted. More or less inconstant symptoms are: fever, probably referable to absorption of toxic products from injured tissues or to localized peritonitis; vomiting due to peritoneal reaction; shock, or transitory syncope. On examination, a mass, ranging in size from that of a small fist to that of the fetal skull, is seen protruding from the wound. Later, the signs of infection may become demonstrable. The presence of the wound in a lower intercostal space or under the border of the ribs, as well as the reddish brown coloration and hard consistence of the mass, point to the spleen. In long-standing cases, the protruding mass may be mistaken for omentum which has a marked tendency to protrude from penetrating abdominal and thoracic wounds. Biopsy may be resorted to in uncertain cases.

Prognosis.—The prognosis is always grave, yet the outlook in these cases is necessarily modified by a number of factors, such as the time of intervention, degree of protrusion of the organ, contamination, de-

gree of strangulation and associated lesions, especially prolapse of other viscera. In partial prolapse of the spleen, it is impossible to ascertain the condition of the portion left in the abdominal cavity, which, as pointed out by Segré, may have sustained injuries capable of giving rise to secondary internal hemorrhage.

Treatment.—The treatment of prolapse of the spleen is essentially surgical. Prompt intervention is indicated, splenectomy in general being the procedure of choice. This operation has been frequently performed in cases of this kind, and usually with a successful outcome, so that it may be described as the ideal treatment. In very recent cases of not more than one to four hours standing, in which the prolapsed spleen is not wounded or grossly contaminated, reduction may be resorted to, according to Gourrin, under strict aseptic precautions. This, however, should never be done unless it can be definitely established that there is no bleeding after the reduction. Such cases should be drained on account of the probability of local infection. Although replacement of the organ will be justifiable occasionally, such treatment involves greater risk of infection than does splenectomy. The return of a partially prolapsed spleen into the abdominal cavity is furthermore dangerous because lesions may be present which do not bleed by reason of the constriction of the external wound margins, but may lead to internal hemorrhage after the constriction has been released. These dangers are lessened by removal of the organ. Février, in 1901, collected thirty observations on traumatic hernias of the spleen, all of which were treated by splenectomy and had a favorable outcome.

Expectant measures are not advisable on account of the danger of infection due to the exposure of the prolapsed organ. Yet, on the basis of recent war experiences, some surgeons favor such treatment. This attitude is supported by Segre and Picqué, whose observations show that hernia of the spleen, like cerebral hernia, is capable of gradual spontaneous reduction. According to Segré (1918), the lesions of the prolapsed spleen have been studied in animal experiments, histological specimens examined at the end of eighteen hours presenting no severe pathological changes except considerable new formation of blood-cells and a low degree of capillary infarction.

In most cases, an independent incision will be advisable, though in some, the original wound may be such as to warrant splenectomy through it after its edges have been excised and the wound extended if necessary. Whenever possible, especially in complete prolapse, the pedicle should be ligated and divided through an independent incision without reducing the prolapsed organ, the spleen being removed through the original wound. The edges of this wound should then be excised and sutured, with or without drainage as seems indicated. But in general, the peritoneum should be sutured and drainage introduced to it.

The results following conservative treatment are illustrated by case

reports where the patients were far removed from surgical aid. Some of these are presented more as curiosities than as being of practical value.

A case of prolapse of the spleen through a wound of the abdomen described by Brown of Darbhanga, India, in 1897, concerned a native thirty-five years of age, the left side of whose abdomen had been ripped open by a wild boar. The uninjured spleen prolapsed through a large oblique wound extending in the axillary line from the tenth rib to the crest of the ileum. He was sent to the hospital, where he arrived four weeks after the accident. At that time, the spleen projected from the side of the body like a huge fungus, completely overlapping on all sides the opening through which it had escaped; it was about two and a half times its normal size. The union of the spleen with the cutaneous surface was very firm. The mass was removed with scissors, after application of strong silk ligatures to the pedicle. The ligatures came away twenty-six days later, and the patient's recovery was uneventful.

St. John Moses, Bengal, in 1889, successfully excised the partially prolapsed spleen of a Mohammedan, forty-five years of age, who had received a severe wound, inflicted by a sharp-edged weapon, in the left hypochondriac region. Between the lips of the wound two and a half inches in length and three quarters in width, was a dark congested mass, a portion of the spleen. The lips of the wound had contracted tightly around the base of the projecting portion, so as to prevent the return of venous blood. The capsule of the organ was incised to the extent of one and a half inches and the splenic pulp was seen bulging through the opening. After catgut ligatures had been applied to the pedicle, the entire spleen was cut away. It weighed twelve and one half ounces and had a slight constriction around the part that had been held by the abdominal wound. A fortnight after the operation, the wound had completely healed and the patient made a speedy recovery. Ten months later he was in good health. Klinger, Serbia, 1888, reported a similar case.

A case of herniated spleen through an abdominal wound was reported in 1905 by Norman White, Civil Surgeon in Chakdara, India. The patient, a young native about twenty-two years of age, was shot in the abdomen at a range of about one foot; the gun was loaded only with powder and a wad, but produced a very severe wound of the abdominal wall. Profuse and continuous vomiting of bile-stained fluid followed, and, as a result of the excessive strain, the spleen began to bulge out of the wound. The patient did not reach the hospital until five days after the accident. One and a half inches above the umbilicus, just to the left of the midline, was a large, irregularly oval, jagged wound with sloughing margins about three inches in diameter through which protruded a portion of a much enlarged spleen. The wound rapidly healed and the patient made an uneventful recovery. The observer comments on the useful part played by the spleen in this case,

where undoubtedly it was a factor in preventing the onset of general peritonitis, so effectually did it block the wound.

Oks, in Odessa, 1879, reported a remarkable recovery under conservative treatment after partial prolapse of the spleen, the patient being a woman of seventy years, who was gored by a bull. A wound 7 cm. in length with lacerated margins was found on the left side corresponding to the tenth intercostal space, and from it protruded a compact dark mass, representing the lower border of the spleen. The herniated segment, which protruded about two fingers' width from the wound, was wiped with carbolic solution and replaced; the wound margins were then united with interrupted catgut sutures. No reaction followed and the abdominal wound healed by first intention.

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CHAPTER VI

CLASSIFICATION OF SPLENOMEGALY, ABSCESS OF THE SPLEEN, CHRONIC PASSIVE CONGESTION, CIRRHOSIS OF THE LIVER, HEMOCHROMATOSIS BERIBERI AND SCHISTOSOMIASIS

CLASSIFICATION OF THE FORMS OF SPLENOMEGALY

In the course of its reaction to pathologic conditions, the spleen generally increases in size. In fact one may say that, with the exception of traumatic conditions, the diseases in which surgery of the spleen demands consideration are almost uniformly characterized by splenomegaly. Attempts to construct a satisfactory classification of the forms of splenomegaly have so far been unsuccessful. Similar pathologic pictures may be found in diseases which are apparently not related, such as syphilis, cirrhosis of the liver and splenic anemia. Different instances or different stages of the same disease may show pictures that are quite different, as for example in splenic anemia. Most of the diseases under consideration are obscure in etiology and pathogenesis, and possible relationships between them have not been recognized. For these reasons, an arrangement upon a strictly etiological or pathological basis or a purely clinical foundation cannot be made satisfactorily.

A classification on the basis of size alone can readily be made but is not of much service. Splenomegalies have been divided into three groups, the small, the medium and the large. The small weigh from 250 to 500 gm. and are found in chronic passive congestion, acute infections and amyloid degeneration. The medium-sized splenomegalies weigh between 500 and 1,000 gm. and are found in chronic malaria, cirrhosis of the liver and Hodgkin's disease. The large spleens are those which weigh more than 1,000 gm., sometimes as much as 7 kg. They are seen in myelogenic leukemia, splenic anemia and Gaucher's disease. An arrangement of the principal forms of splenomegaly in the order of their size might be made as follows:

Gaucher's disease	Polycythemia
Myelogenic leukemia	Acute infections
Splenic anemia	von Jaksch's anemia
Lymphosarcomatosis	Rickets
Chronic malaria	Chronic congestion
Hodgkin's disease	Amyloid degeneration
Hemolytic icterus	Syphilis
Cirrhosis of the liver	

But any such list is subject to many individual exceptions. The spleen in cirrhosis of the liver or in syphilis may at times be very large, and in all conditions the size of the organ depends upon the stage of the disease.

The classification which we present here has no uniform basis, it is not brief and it requires many explanatory notes, but it has been helpful.

I. Acute splenomegaly occurring in acute infections.

1. Acute congestion, occurring in the early stages of many acute infections.
2. Acute splenitis (septic spleen or acute splenic tumor).
3. Acute suppurative splenitis.
4. Abscess of the spleen.

II. Chronic splenomegaly due to chronic passive congestion together with varying proportions of changes resulting from the activity of some toxic factor.

1. Chronic cardiac disease.
2. Chronic pulmonary disease.
3. Cirrhosis of the liver.
4. Beriberi.
5. Schistosomiasis.
6. Pylethrombosis.

III. Chronic splenomegaly associated with chronic infections. Three types may be recognized.

- A. Due to recurring attacks of splenitis resulting in hyperplasia and fibrosis.
 1. Syphilis—diffuse form.
 2. Chronic malaria.
 3. Kala-azar.
 4. Other types of tropical splenomegaly.
- B. Due to the development of granulomatous tissue in the spleen.
 1. Syphilis—gummatous form.
 2. Tuberculosis.
 3. Hodgkin's disease.
 4. Leprosy.
 5. Glanders.
 6. Actinomycosis.
- C. Amyloid degeneration of the spleen.

IV. Chronic splenomegaly which appears as one manifestation of disease involving the hematopoietic system.

1. The anemias.
 - a. Simple anemia.

- b.* von Jaksch's anemia.
- c.* Splenic anemia.
- d.* Pernicious anemia.
- 2. The leukemias.
 - a.* Myelogenic leukemia.
 - b.* Lymphatic leukemia.
 - c.* Anomalous leukemias.
 - d.* Pseudoleukemia.
- 3. Polycythemia vera.
- 4. Hemolytic icterus.
- 5. Gaucher's disease.
- 6. Telangiectatic splenomegaly (Symmers).
- 7. Rickets.

V. Cyst of the spleen.

Nonparasitic.

- 1. Large, usually single, for the most part due to hemorrhage.
- 2. Small multiple—of no surgical significance.
- 3. Polycystic degeneration.
- 4. Dermoid.

Echinococcus.

VI. Neoplasms (primary) of the spleen.

- 1. Benign tumors of connective tissue origin.
- 2. Angioma.
- 3. Malignant tumors of connective tissue origin.
 - Fibrosarcoma.
 - Lymphosarcoma.
 - Large-celled endothelial sarcoma.

I. All of the conditions in Group I may be considered as different stages of one process. The lesion is essentially a combination of acute congestion and diffuse hyperplasia of the pulp to which is added, in the more extreme forms, leukocytic infiltration and necrosis.

II. Group II contains a number of unrelated conditions, but the histologic picture in all of them has certain elements of similarity. There is a good argument for the inclusion of splenic anemia in this group, both on account of its pathology and its supposed close relation to cirrhosis of the liver. But its place has been so firmly fixed among the anemias by custom that we have not felt justified in changing its position.

III. Group III is rather more logical in its composition. Hodgkin's disease is generally believed to be infectious in nature. Amyloid degeneration is quite different from the other conditions but clearly belongs in the group.

IV. Group IV is a satisfactory one on the basis of a uniformity of system involved. But it includes diseases that are obviously wholly unrelated. Several of the forms of anemia are probably merely symptom complexes and in time will be more accurately identified. Gaucher's disease is quite different in its nature from most of the conditions included in this group.

Rickets has been included because of its close relation to anemia in general and to von Jaksch's anemia in particular. The bone changes in rickets are believed to have some influence upon the bone marrow and therefore upon the hematopoietic system.

ABSCESS OF THE SPLEEN

Although abscess of the spleen is an infrequent lesion, it occurs far more often than operative statistics indicate, by reason of the fact that surgical intervention is rarely undertaken. As a complication of infectious diseases, it is frequently overlooked. Doubtless it will become more often recognized and operated upon, as has been the case in suppurative pericarditis, as attention comes to be focused more upon this organ as the possible site of a suppurative process.

The *etiology* is variable, yet the condition usually occurs as a metastatic abscess; occasionally, lowered resistance from traumatism is a predisposing factor (infected hematoma); rarely the abscess develops as a direct extension of an adjacent suppurative process, for instance from the liver; finally, in a considerable proportion of cases there is no demonstrable cause.

The first group, namely, metastatic abscesses, demands some elaboration. Any infectious disease may be the cause of a secondary splenic abscess, but especially typhoid, puerperal sepsis, pyemia and localized suppurative processes, such as carbuncle and appendical abscess. It has been reported also as occurring after measles, small-pox, influenza, dysentery, diphtheria, ulcerative endocarditis, yellow fever and relapsing fever. Kernig in 400 cases of relapsing fever observed 5 cases of abscess of the spleen; Petrowsky reported 5 cases of spleen abscess in relapsing fever. Ponfick, in a series of autopsies, 1872-1873, on relapsing fever patients in one epidemic, found infarcts of the spleen in 40 per cent of the cases. Pikin, in 1919, observed 29 instances of splenic infarction and necrosis among 53 autopsies on persons who had died from relapsing fever. This material included 3 ruptures. While abscesses have occurred in leukemia and malaria, these conditions may be regarded as predisposing factors only in so far as they diminish the resistance of the organ to infection. The relative frequency of abscess formation in malarial spleens is questionable. Chowdhooory, in India, observed only 3 cases in 30,000 cases of malaria. Anderson reports that in 77,949 cases of malaria, only 2 cases of abscess of the spleen were

recognized during life. In the last 178 fatal cases of which postmortem records were available he found 3 cases with splenic abscess.

Staphylococci, streptococci and typhoid bacilli are the organisms most frequently found. But, as Elting states, practically all the pyogenic bacteria except the gonococcus have been described as occurring in such abscesses, notably, in addition to those mentioned, *B. coli communis*, *Pneumococcus*, *B. pyocyaneus* and *Proteus mirabilis*. The Eberth bacillus as a rule is responsible for splenic suppuration as a sequel to typhoid fever, and may be found in pure culture. In some cases, the pus derived from splenic abscesses has been found to be sterile on bacteriologic examination. Stuckey reported a sterile culture in a case of abscess occurring in relapsing fever. Cutler's case, secondary to bilateral otitis media, gave no growth. Why the organisms in the circulation are arrested and develop in the spleen is unknown. Some writers, notably Litten and Elting, consider that thrombotic infarcts are the rule; others believe that the suppurative process may originate without antecedent infarcts. Küttner (1907) presented some interesting work in connection with the production experimentally of splenic abscesses. The abdomens of rabbits were opened, the spleens squeezed at their upper and lower poles, abdomens closed and culture of *Staphylococcus aureus* injected into the veins of the ears. At autopsy, the contused portions of the spleens were found to be a mass of pus. In the unsqueezed portions of the spleens, there were occasional small abscesses but no sequestra. He injected a culture of *Staphylococcus albus*, *aureus* and olive oil into the splenic artery after it had been centrally ligated. Infarction resulted with many bacteria in infarcts and pus infiltration.

Abscess of the spleen appears to be more common in men. Melchior states that in the 11 reported cases in which the sex is mentioned, there were 8 males and 3 females.

Pathological Anatomy.—A characteristic feature of splenic abscesses is their marked tendency to form "sequestra" (Küttner), the pus frequently containing large necrotic shreds or masses of splenic tissue. Exceptional cases have been recorded in which almost the entire organ was detached from its capsule and bathed in pus (Bessel-Hagen). Küttner, in 1907, collected 116 cases of splenic abscess, 2 of which were in his own experience, and of this number 43, or 37 per cent, were of the sequestrating variety. The etiology of these 43 cases was grouped as follows: traumatic origin, 6 cases, 14 per cent; general sepsis, 11 cases, 25.28 per cent; posttyphoid, 6 cases, 13.95 per cent; postmalarial, 7 cases, 16.28 per cent; associated with twisted pedicle of movable spleen, 2 cases, 4.65 per cent; following perforation of the stomach, 3 cases, 6.97 per cent; cases of doubtful origin, 8 cases, 18.6 per cent.

Primary intrasplenic abscesses may become perisplenic through destruction of the capsule, giving rise to left subphrenic abscess, although this is relatively infrequent according to Pikin. In the presence of an

abscess, the organ forms extensive adhesions with the diaphragm and neighboring viscera, especially the stomach and transverse colon. In some reported cases, abscesses have perforated into the stomach, intestine, pleura, peritoneum and on the surface. In a case of Mangiurea, reported by Moynihan, the spleen was expelled as a whole through an orifice at the level of the umbilicus.

Traumatic abscesses of the spleen are nearly always solitary. Embolic abscesses, although originally multiple, often coalesce into a single large abscess through softening and disintegration of the intermediate tissue. The small multiple abscesses of the spleen, noted in the course of pyemia, are devoid of surgical importance. The size of a spleen abscess is not, as a rule, great, rarely exceeding 8 to 10 cm. The pus is blood tinged, of a reddish or brownish, sometimes yellowish color,

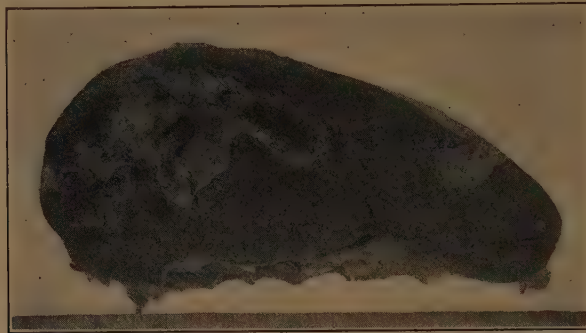


FIG. 30.—ABSCESS OF SPLEEN—PUERPERAL SEPTICEMIA.

Two months before death miscarriage at 2½ months after which patient bled considerably for 2 weeks. Since onset chills, fever and evidence of profound sepsis. Blood cultures negative. Autopsy. Multiple abscesses of spleen and liver, uterus of normal dimensions and firm consistence; pelvic veins, hemorrhoidal and femoral veins, not thrombosed.

and often has an offensive smell. In Litten's exceptional case, the abscess contained fifteen liters of pus (Nothnagel).

Symptoms and Diagnosis.—The fact that these abscesses not infrequently are discovered at autopsy, having remained unrecognized during life, indicates the difficulty which often arises as to diagnosis. The clinical picture of splenic abscess is usually rather indefinite in the beginning, especially when the pus accumulates deep in the substance of the organ. It is not until the capsule becomes involved in the inflammatory process that the presence of the abscess manifests itself by pain. Pain is suggestive only and due to perisplenitis. It is not pathognomonic and may be due to pleurisy or splenic infarcts. It often radiates especially to the left scapular region. Fever of a remittent or intermittent type is a fairly constant symptom, although there are a number of reported cases in which there has not been a significant elevation of temperature. Irregular chills have been noted in most cases. Rapidly growing abscesses in the lower pole of the spleen, in the direction of the abdominal cavity, induce palpable enlargement of the spleen and

well-marked tenderness on pressure. Abscesses in the upper segment often give rise to the symptoms of subphrenic abscess and are apt to be overlooked in consequence of the frequent early involvement of the left pleura. Friction sounds have often been described over the left base and serohemorrhagic fluid has been observed in the left pleural cavity. Suppurative pleurisy may ensue and the original focus may be readily overlooked. The diaphragmatic movements on the left side are often absent, as shown by the X-ray. A local point of tenderness can at times be demonstrated, and slight edema of the lower intercostal spaces is sometimes present. These features suggest the location of the pus focus (Bessel-Hagen, Iversen and Stulern, de Vlaccos). Distinct fluctuation is demonstrated only in the larger abscesses. Blood examination yields no characteristic findings. Leukocytosis of a pronounced character, from 20,000 to 50,000, has been frequently noted and emphasized by some writers as a diagnostic point of great importance. On the other hand, numerous cases are said to have shown no significant increase in the leukocytic count. Therefore, undue diagnostic importance should not be placed upon this feature. A low count does not exclude splenic abscess, while a high count in association with suggestive local signs is strongly corroborative. Examination of the blood may be of great value in typhoid fever, since leukopenia is the rule and an increase in the white blood-cells may indicate a suppurative complication. As the disease progresses, the patient becomes emaciated and presents the picture of profound sepsis.

Differential Diagnosis.—Abscess of the spleen is frequently not recognized. The condition has been confused especially with perinephritic abscess, subphrenic abscess, purulent pleurisy, acute forms of miliary tuberculosis, malarial splenic enlargement and other types of splenomegaly. But such conditions as hydatid or nonparasitic cysts, Banti's disease, etc., can usually, though not always, be differentiated by the absence of a febrile reaction. Purulent pleurisy often accompanies suppuration of the spleen. Perinephritic abscess is lumbar rather than abdominal, and the pain radiates downward instead of toward the left shoulder, as is usual in abscess of the spleen. X-ray examination has been recommended as a diagnostic aid, elevation and fixation of the diaphragm being significant, although they do not differentiate the lesion from subphrenic abscess. The differentiation of splenic abscess from malarial splenomegaly has proved difficult in some cases, since intermittent fever and splenic enlargement belong to both affections. The demonstration of the plasmodium in the blood smear does not, of course, exclude abscess. Exploratory aspiration has often aided in arriving at a correct diagnosis. While this procedure has been decried by some observers (for example, Spear), the majority believe that it is a justifiable diagnostic method. Melchior collected 17 cases of abscess of the spleen following typhoid fever, in which exploratory aspiration was practiced without untoward effects. In one case, several punctures were made

through the intact pleura before pus was found in the spleen and no ill results followed. Of course operation should always be undertaken soon after a positive puncture. Yet in one of Melchior's cases, there was an interval of thirteen days. Even in this case there was no infection of the pleura.

It is quite evident that had exploratory puncture been used at an earlier stage of the disease, many cases that have been lost might have been correctly diagnosed and successfully treated. On the other hand, in many cases the surgical indications should be recognized early without aspiration. In this event, an exploratory operation should be undertaken. In a septic case with evidence of suppuration beneath the diaphragm, there may be no necessity for puncture. The use of exploratory puncture, then, should be restricted to carefully selected cases.

Prognosis.—In the absence of timely surgical intervention, the prognosis of abscess of the spleen is unfavorable; on the other hand, early operation is often followed by excellent results. This is notably the case in typhoid abscess. Stuckey reported only 2 deaths in 22 cases of post-typhoidal abscess that were operated upon, a mortality of 9 per cent, in contrast to a mortality of 21 to 23 per cent in abscess of the spleen from all causes. Death in neglected cases may be due to general sepsis, cachexia, or some complication, such as peritonitis or intestinal obstruction. In other cases, death has followed rupture of an abscess into the splenic vein. At times, however, the infection remains localized for a long period. Thus, Wallace reports a case in which the spleen almost filled the abdomen. It was adherent to the abdominal wall and incision evacuated four quarts of pus. The patient recovered. Wallace had a large experience with South African natives and reported 19 operated cases, with 15 recoveries. However, Pikin's experience in Russia, where splenic abscess occurred as a complication of relapsing fever, indicated that the prognosis is very grave even after early operation.

Treatment.—The treatment is operative; splenectomy or splenotomy. In most cases, splenotomy or drainage of the abscess cavity has been performed, but a considerable number of successful cases of splenectomy for splenic abscess have been reported. Splenectomy should be confined to cases in which the organ can be removed without difficulty or serious risk of peritoneal contamination. The existence of firm adhesions renders splenectomy dangerous. The approach may be transpleural, abdominal or retroperitoneal. In abscesses of the upper pole, which have been localized by exploratory puncture, the transpleural route may be advisable, resection of the ninth, tenth, or eleventh ribs being made with center in the posterior axillary line. If the pleural surfaces are found adherent, as is frequently the case, the diaphragm is incised and the abscess drained immediately, otherwise a two-stage operation is performed. The pleural surfaces are approximated by suturing the diaphragm to the thoracic wall and the abscess is opened

after adhesions have closed the pleural cavity. As Elting states, the transpleural is the shortest, but also the most difficult route to reach the spleen unless the pleural layers are adherent, when it is the ideal method. The abdominal approach is made through any appropriate incision but usually by an incision parallel to the twelfth rib, if necessary with resection of that rib. The spleen is thus readily accessible, especially if the abscess is located in the lower pole. The retroperitoneal route was used by Propping in a reported case. The incision extended from the tip of the twelfth rib forward along the costal margin. The oblique muscles were cut and the finger introduced in the retroperitoneal tissues along the diaphragm until the abscess was reached and drainage established.

Since the diagnosis is not always positive, operation may be of an exploratory nature. In such a case, a vertical left rectus incision may be employed for exploration and the abscess opened and drained through a counter opening below the twelfth rib. A persistent fistula, after splenotomy, may indicate the performance of a secondary splenectomy.

The following illustrative case was reported by Elting. The patient was a woman twenty-seven years of age. A short time before the onset of her illness an abortion had been performed. On June 11, 1914, while apparently in good health, she was suddenly seized with a sharp pain in the left upper quadrant of the abdomen. The pain radiated to the back on the same side; the patient was nauseated but did not vomit. The urine was blood tinged. From June 14 to 17 she improved, but on June 18 the pain became much more severe, especially over the left lower quadrant of the abdomen, radiating to the back, and a moderate amount of blood appeared in the urine. The pain was not affected by respiratory movements. There was tenderness over the left upper abdominal region and some abdominal distention. The urine showed a trace of albumin and a few red blood corpuscles; the leukocytes were 19,000. On June 22, radiographs of the lower chest and abdomen were negative. During the succeeding days, the patient was troubled with nausea and vomiting, intestinal distention, and abdominal unrest. From June 20 to June 30, the patient's temperature was irregular, ranging from 98.6 to 102.4, and the leukocytes ranged from 20,000 to 24,000. The area of splenic dullness increased and pressure over this area was painful. On July 1, the temperature fell to normal, and for six days there was practically a disappearance of all symptoms except some slight pain. On July 7, the temperature rose to 102.6; there was recurrence of all the symptoms; the leukocytes were 22,400; the temperature assumed a remittent septic type and the spleen could be palpated 2 cm. below the costal margin. On July 17, there was dullness in the mid-axillary line extending upward to the ninth rib. Exploratory aspiration was done through the ninth interspace in the posterior axillary line and only blood obtained. On August 4, a radiograph showed an arching upward of the diaphragm on the left side. Both pleural cavities

were normal. Exploratory aspiration was employed in the tenth interspace posteriorly, and pus was located at a considerable depth. A portion of the eleventh rib was resected posteriorly and a small abscess, deeply seated, below the diaphragm, was opened. The pus showed a pure culture of pneumococci. On August 27, the patient complained of pain in the liver region and the liver was found to be somewhat enlarged and rather sensitive. On August 29, freer drainage appeared desirable, a considerable area of the tenth rib was resected and the spleen was found to be riddled with abscesses, with some areas of sequestered splenic tissue, the largest of which was the size of a walnut. The patient's condition grew steadily worse. She complained of pain over the liver and this organ became much enlarged, with some icterus. On September 20, she died. An autopsy was not obtained.

Elting states that the uterus, intestines and left kidney must be regarded as the possible source of infection. When the abscess was finally located by radiography and aspiration, the infectious process had gone too far to be favorably dealt with by surgery. He also states that, had an exploratory laparotomy been done in the earlier stages of the disease, a more favorable outcome might have been obtained.

Splenic Abscess in Typhoid Fever.—The fact that typhoid fever is the most frequent cause of abscess of the spleen indicates a more detailed review of the complication as an incident of that disease. Its occurrence may be explained by infarcts and foci of necrosis which are often present in the spleen in typhoid. For instance, Curschmann found 25 cases of infarct in 577 autopsies upon typhoid patients in Hamburg and Leipzig hospitals, while in the same 577 autopsies he noted 4 splenic abscesses, 0.7 per cent. Berg's statistics from the Leipzig clinics (1880–1893) comprise 1626 cases; 243 of these died, and 228 came to autopsy; splenic abscesses were found in 4 instances, a frequency of 0.25 per cent of the clinical material (quoted by Melchior). The same proportion results from the statements of Vierhuff, from the Riga City hospital, where clinical material of 1,186 patients, with a mortality of 112, included 3 splenic abscesses.

Piorkowsky's statistics are somewhat surprising. He reports no abscesses. The figures are based upon the cases of typhoid at St. Jacob's hospital, Leipzig, from 1893 to 1907. The cases numbered 1,229 with a mortality of 231. Infarctions were found 6 times and necrosis of the spleen 3 times.

Webb-Johnson reported 3 cases of splenic abscess in his series; 1 in the course of typhoid (an inoculated man), and 2 in paratyphoid B, neither of them inoculated.

The *Bacillus typhosus* often may be recovered from the pus. In 20 operated cases, Stuckey reports that in 12 the pus obtained by puncture was cultured. In 8 cases, there was a pure growth of *B. typhosus*; in 1, *B. coli*; in 1, *Streptococcus*; in 1, *Streptococcus* and *Staphylococcus aureus*; in 1, *Proteus mirabilis*. In 4 cases not operated upon, a pure culture of

B. typhosus was found in 3; in 1, *B. typhosus* and *Staphylococcus aureus*. In a case reported by Kirchmayr (1906), typhoid bacilli were grown in pure culture from the pus of a splenic abscess which had formed as a sequel to a very mild case of typhoid fever in a woman twenty-seven years of age. While in some cases pyogenic organisms only have been isolated, in others no organisms have been demonstrable.

The intensity of the typhoid is not an index to the probability of abscess development. On the contrary, Melchior states that abscess is more frequent after mild cases. There is often an interval without fever between the typhoid and the onset of symptoms due to the abscess.

Webb-Johnson's 3 cases are of interest. The patient with typhoid died on the twenty-second day. At autopsy, suppurating infarcts were found in the spleen with an abscess on the surface. *B. typhosus* was grown from the pus. One of his paratyphoid cases died on the twenty-third day from perforation of the sigmoid flexure. At autopsy, 2 abscesses were found in the spleen, each the size of a pigeon's egg. *Bacillus paratyphosus B* was grown from the pus. The other case died on the thirty-sixth day. At autopsy, the intestine, including the appendix, was normal in appearance. The spleen was found to be adherent to the parietes, to the colon, and to other viscera. There was an abscess the size of a plover's egg in the lower pole, and there were other smaller abscesses towards the hilum of the organ. *Bacillus paratyphosis B* was isolated from the pus obtained from these abscesses.

Melchior describes the symptoms as follows: the first intimation of abscess formation is usually pain in the left hypochondrium, of sudden onset and considerable severity. Sometimes the pain is aggravated by deep breathing or coughing. Occasionally the pain may be localized, at first in the lower abdominal region, or it may radiate toward the left shoulder; but, as a rule, the pain is purely local. Fever and chills may manifest themselves either suddenly or gradually, and vomiting has been observed in isolated instances.

The objective signs present noteworthy variations, according to whether the abscess develops in the lower pole or, as is more commonly the case, in the upper pole of the organ. In the former, enlargement of the spleen will soon become demonstrable on palpation, the splenic swelling sometimes extending considerably below the costal arch. Muscular rigidity between the costal arch and the iliac crest is suggestive of involvement of the peritoneum. When the upper pole of the spleen is affected, palpation often fails to reveal distinct changes and only an enlarged and progressively increasing splenic dullness is demonstrable. Peritoneal friction is sometimes noted over the organ. Tenderness on pressure in the region of the spleen is not uncommon; in other cases, there may be tenderness on percussion of the left lower thoracic region. In still other cases, palpation of the splenic region is described as quite painless.

In contradistinction to abscesses situated in the lower pole, those which develop in the upper pole seem to possess an extremely marked tendency to early perforation of the splenic capsule with evacuation of the abscess contents into the left subphrenic space. All these cases, accordingly, represent secondary subphrenic abscesses. In some of the cases, the pleural space is diminished in size, through the ascent of the diaphragm, while in others it has itself become the seat of an exudate, through the extension of the inflammatory process to the pleura. X-ray examination is strongly indicated and may be expected to reveal, in a considerable proportion of cases, elevation and fixation of the left dome of the diaphragm.

In typhoid fever, a rise of leukocytes is suggestive of a suppurative complication.

When there is a strong suspicion of splenic abscess, exploratory puncture is justified, though there are some disadvantages which have been discussed under abscess of the spleen. Webb-Johnson gives the following instructions: a fine long needle is used. The puncture is made in the tenth intercostal space in the midaxillary line. The patient is recumbent as a rule, but the puncture may be made with the patient in a sitting position, with the left arm raised. He should be instructed to hold his breath, and the aspiration should be done quickly. In case the patient makes respiratory movements, the needle should not be fixed, but should be supported and allowed to follow the movements of the spleen.

The prognosis in typhoid abscess is much better than that of abscess from other causes, probably because of the relatively low virulence of the infection. Thus, there were only 2 deaths in 22 operated cases collected by Stuckey.

One of Webb-Johnson's cases of paratyphoid, B., presented an interesting history. On the twenty-second day, he complained of pain in the lower part of the left side of the chest on taking a deep breath. This passed off, however, and there was improvement in his general condition until the thirty-fourth day, when he vomited and the temperature rose to 102.6 and pulse rate to 128. Later he complained of pain in the left hypochondriac region, and the abdomen became tender and rigid. His general condition grew rapidly worse, and he died on the thirty-sixth day.

CHRONIC PASSIVE CONGESTION OF THE SPLEEN

Because of its intimate relation with the circulation and on account of its elastic capsule, the spleen is exceedingly sensitive to many of the changes which take place in the circulatory apparatus. Congestion appears as soon as the right ventricular muscle begins to be inadequate for its task, and as the cardiac insufficiency persists and progresses, the spleen exhibits those changes which characterize chronic passive con-

gestion, chronic stasis or cyanotic induration. If this condition is present over a long period of time, the picture in the spleen gradually changes from congestion to atrophy and the condition known as cyanotic atrophy is found.

Etiology.—The immediate cause of this type of chronic passive congestion is found in failure of the cardiac muscle. The cause of cardiac failure may be one of a number of conditions. In the spleen in this condition, we find more nearly a pure chronic passive congestion than in any other. Nevertheless we cannot say that the changes are due solely to mechanical influences. As the rapidity of the circulation becomes less, the tissues are deprived of a certain fraction of their accustomed supply of food and oxygen and are unable to rid themselves completely of their waste products. Diminished oxidation favors the development of certain degenerative processes and some of the waste products are toxic in their action. Thus the picture found in the spleen is probably the combined effect of mechanical and chemical influences.

In considering the pathology of this condition, it is necessary to bear in mind the fact that cyanotic induration of the spleen is seen only at autopsy. Patients with cardiac insufficiency are rarely operated upon so that we have no data as to the condition of the spleen during life. With cessation of the circulation, the spleen must lose a large proportion of the blood it contains and thus become smaller and harder.

Cyanotic induration of the spleen has been briefly described in the section on pathology. The organ is moderately enlarged, rarely weighing more than 400 gm. Its form is well preserved though the margins are often somewhat rounded. The color is dark bluish red and the capsule is smooth and moderately tense. The consistence is very hard and is often described as being "as hard as a board." On section, the cut surface is dark red, smooth and rather moist, though the pulp is not readily scraped from it. The capsule and trabeculae are not obviously thickened. The pulp appears to be homogeneous. Usually the follicles are readily visible and are normal in size and numbers. In long-standing cases, they may be compressed and finally disappear.

Microscopic examination reveals the presence of a surprisingly small increase in the fibrous tissue content of the spleen, when one considers its extreme hardness in this condition. The capsule, trabeculae and the pulp reticulum all show but moderate increase in thickness. It is stated that in stasis of central origin there is no extension of elastic fibers into the pulp. The pulp cords and the lymphoid tissue show little or no deviation from the normal. The striking feature in the picture is the tremendous engorgement of the spleen with blood. The venous sinuses are widely, though rather irregularly, dilated and their walls may be recognized only with difficulty. The pulp tissue is markedly infiltrated with red blood-cells and the whole appearance has been called that of a blood lake.

When cardiac insufficiency has persisted for a long period, the pic-

ture of cyanotic induration gradually disappears, atrophic changes appear and we have the lesions of *cyanotic atrophy*. The spleen is smaller than in stasis and the capsule is wrinkled but the color is still distinctly bluish. The consistence is not so hard but is very tough. On section, the capsulotrabecular system shows definite thickening and the malpighian bodies are small or absent. The cut surface is not quite as dark as in stasis and is appreciably drier.

On microscopic examination, there is seen distinct thickening of the capsule and trabeculae and also of the walls of the venous sinuses. The reticulum may exhibit hyaline degeneration. The amount of blood in the spleen is still greater than in the normal organ but is much less than we have seen in chronic passive congestion. The follicles are compressed or there may be complete absence of definite follicular structure. The pulp remains normal.

The *symptoms* found in this condition are those of the cardiac insufficiency and its causes. None are directly referable to the spleen. The spleen may be palpable, but in a large percentage of these cases its enlargement is not sufficient to permit of its being felt.

The *treatment* is that of the cardiac insufficiency and its cause. Venesection, digitalis and rest are the most important measures. The part which the spleen plays in the process is an unimportant one and no treatment directed to the condition in this organ is necessary.

CIRRHOSIS OF THE LIVER

At one time the view was generally held that the enlargement of the spleen so frequently seen in cirrhosis of the liver was of no more significance than that found in chronic cardiac or pulmonary disease, and many believed that it was of the same nature. In more recent times, the conception of cirrhosis of the liver has undergone considerable change and with this change has come the assignment of the accompanying splenomegaly to a position of more importance.

The name cirrhosis was first given to the portal type of the condition because of the yellow color of the organ. Later there were included under this term other changes in the liver characterized by marked increase in its connective tissue content. On a pathological basis various subdivisions of cirrhosis have been made, as Laennec's cirrhosis, Hanot's cirrhosis, obstructive biliary cirrhosis, hepar lobatum and cirrhose cardiaque. But there is a modern tendency, especially among the clinicians, to simplify this classification. Hepar lobatum and cirrhose cardiaque are dropped from the group since they are considered to be not true examples of cirrhosis. The other types, which show intermediate forms and cannot always be differentiated clinically, are brought into two groups, the portal and the biliary cirrheses. The conception of Hanot's cirrhosis has been revised entirely. Mayo believes it to occur in two

forms, one being an obstructive biliary cirrhosis and the other a hemolytic icterus with work hypertrophy of the liver.

What is more important is the attack upon the advisability of considering cirrhosis of the liver as a disease entity. The subject has recently been reviewed by Epplen. He says: "Cirrhosis of the liver is a chronic, recurring, probably focal, possibly diffuse degeneration or necrosis of the parenchymatous cells of the liver, modified by concurrent and intercurrent periods of regenerative proliferation of the parenchyma, with connective tissue replacement of the destroyed areas. Acceptance of this definition and any concept that cirrhosis of the liver is a disease entity are incompatible." He thinks it reasonable to assume that the end result called cirrhosis of the liver may be produced by a variety of primary clinical processes. A consideration of the relation of cirrhosis of the liver to certain other conditions has led him a step further. Splenic anemia, with its terminal syndrome known as Banti's disease, is undoubtedly closely related, both clinically and pathologically, to hepatic cirrhosis. There are a number of writers who have expressed the opinion that the two conditions are identical. In hemachromatosis, there is close association of liver cirrhosis with a metabolic disturbance. Urobilin jaundice is common to cirrhosis of the liver and both pernicious anemia and hemolytic icterus. Hypertrophic cirrhosis bears a close resemblance to hemolytic icterus and the liver enlargement is called a work hypertrophy in this disease. In view of these resemblances, Epplen feels that when dealing with cirrhosis of the liver we must regard it as being closely allied to diseases of the blood.

We are not yet ready to follow this path to its logical termination, however attractive it may seem at its beginning. The matter is as yet almost wholly speculative. But the older theories offer no helpful solution to the obscurities which surround the nature of these diseases, and the newer ones promise more.

Splenomegaly is practically constant in all forms of hepatic cirrhosis. Sometimes it develops late and sometimes early. In fact it sometimes appears so early that the spleen may be felt long before there is any evidence of involvement of the liver. Whether this is actually a "pre-cirrhotic splenomegaly," as it has been described, is doubtful. Changes in the structure of the liver must precede their recognition by a considerable period, and some of the cases would probably be considered as examples of splenic anemia. Nevertheless, splenomegaly is evident in a certain proportion of cases before there is any evidence of obstruction to the portal circulation and therefore may be considered as not due to chronic passive congestion.

Since it seems certain that splenic enlargement is not necessarily secondary to the development of cirrhosis in the liver, the question arises whether the spleen is affected coincidentally with the liver by those factors which produce the disease or conceivably harbors the exciting cause of hepatic cirrhosis. It has never been shown that the spleen is

a center for the production of toxins, whether for the cause of liver cirrhosis or any other disease and, while it is attractive to attribute the improvement which may follow splenectomy in cirrhosis of the liver to the removal of the source from which toxic materials are supplied to the liver, such an explanation must be considered purely hypothetical. We are more inclined to believe that the factors which produce cirrhosis in the liver also are capable of causing changes in the spleen and that one organ or the other is affected first or predominantly, depending upon variations in the several factors involved.

Laennec's portal, atrophic, annular or alcoholic cirrhosis of the liver has always been associated in the minds of the profession with the abuse of alcohol. Cirrhosis of the liver has been produced experimentally in animals by the administration of alcohol and this poison appears to be the greatest single factor in the causation of the disease. But only a small percentage of chronic alcoholics develop cirrhosis of the liver, and it is not rare to find a patient suffering from cirrhosis of the liver in whom alcohol can definitely be excluded as an etiological factor. In these cases the cause is admittedly unknown.

The liver may be somewhat enlarged early in the disease, but at autopsy it is usually smaller than normal. The surface is yellowish or brownish and roughened by the projection of irregular nodules which give the organ the appearance which has been designated "hob-nail liver." On section, the cut surface is yellow or brownish or, occasionally, stained green with bile. The liver is seen to be traversed by bands of connective tissue of varying widths which separate small islands of liver tissue of a more or less normal appearance. On microscopic examination these islands are found to be of two varieties. In one, the liver cells are arranged normally but many of the individual cells show fatty or parenchymatous degeneration. These are the cells which are dying. In the other variety, the individual cells appear to be normal but their arrangement is disorderly and abnormal. These are considered to be groups of regenerated cells. In the connective tissue are found groups of newly formed bile ducts. In the regenerated islands, the "central" vein is often placed eccentrically. Injection experiments have shown that the areas of newly formed liver tissue receive blood only from the hepatic artery, while the degenerating lobules retain their normal relationship with the portal vein (Epplen). Not infrequently there is marked fatty degeneration of the liver as well, and in these cases the liver is larger than it would otherwise have been.

Hanot's cirrhosis was originally described as hypertrophic cirrhosis with jaundice, characterized by a chronic intermittently febrile course, jaundice without clay colored stools, and the absence of ascites. The liver was said to be large and to show marked intralobular development of connective tissue. Later a capillary cholangitis was added to the pathologic picture. As we have said, this idea of the condition has been altered. Epplen divides Hanot's cirrhosis into two forms.

First, those cases in which a degenerative process in the liver is associated with a toxic jaundice and which resemble Mayo's hemolytic icterus with work hypertrophy of the liver. Second, cases of jaundiced hypertrophic cirrhosis associated with intense capillary cholangitis in which the connective tissue shows no tendency to contract and the etiology is "clearly infectious." This second type of Hanot's cirrhosis should be included in the group of biliary cirrhoses, nonobstructive.

Obstructive biliary cirrhosis is a rare type, probably because in these days early surgical interference prevents its development. The liver is small, very hard and dark green in color. Chronic infection appears sooner or later. The liver shows intense bile stasis and destruction of liver cells. The normal lobular structure is preserved. The connective tissue is gathered chiefly about the bile ducts and capillaries and is associated with the usual evidences of inflammation.

The spleen in portal cirrhosis is practically always large and may weigh as much as 1,600 gm. The average weight is said to be about 400 gm. It is larger than the spleen of chronic passive congestion and not so hard, being rather firm and tough in consistence. The capsule is thickened and may be wrinkled and there is often more or less perisplenitis. On section, the cut surface is a grayish red. The pulp often bulges somewhat and can be scraped off more readily than in chronic passive congestion. The follicles are apt to be few and small or invisible to the naked eye. On microscopic examination there is found but moderate congestion. There is an increase in the connective tissue content and a hyperplasia of the pulp with later atrophy of the follicles. Hemosiderin is practically always found. The lesion is essentially an interstitial splenitis and differs chiefly in degree from that found in splenic anemia (Banti's syndrome). More detailed comment on these differences will be found in the section on splenic anemia.

In the hypertrophic cirrhoses, the spleen is even larger than in the portal variety. It shows similar changes except that the fibrosis is more marked.

Cirrhosis of the liver is a chronic disease, but invariably terminates fatally unless the patient dies previously of some intercurrent infection or other condition. Known etiologic factors (alcohol, spices, etc.) may be removed and, by means of careful diet, the life of the patient may be prolonged. Certain of the symptoms may demand treatment. Hemorrhages from the gastro-intestinal tract may be so severe as to require transfusion or other treatment of the acute anemia. When portal obstruction has appeared, ascites may require tapping of the peritoneal cavity or it may seem desirable to perform some operation such as Talma's, uniting the omentum to the abdominal wall in an effort to avoid the necessity of frequently repeated tapings.

The most severe and threatening symptoms of cirrhosis of the liver are associated with the obstruction to the portal circulation. These are the gastro-intestinal hemorrhages and the ascites. The

removal of the spleen has been suggested to relieve the burden of this circulation on the liver. Under normal conditions, it has been estimated that the spleen furnishes about fifteen to twenty per cent of the blood brought to the liver by the portal vein. When the size of the spleen is increased four or five times, this percentage is definitely increased. The removal of this organ will then effect a definite reduction of the mass of blood brought to the liver and enable it to function in an approximately normal fashion even though seriously injured. The further argument has been added that splenectomy might remove from the body an organ in which toxic materials are produced and thus would benefit the liver for that reason. The possibility of the influence of a combination of materials from the spleen with others from the intestinal tract has received but little attention. It probably deserves as much consideration as does the toxin of splenic origin. With the relief of the burden upon it, the liver, by the exercise of its known regenerative powers, may actually increase its functional capacity.

Splenectomy has been performed a number of times in cirrhosis of the liver. The largest series of cases has been reported from the Mayo Clinic by Giffin. They have removed the spleen in 10 instances of portal cirrhosis and 6 cases of biliary cirrhosis. In biliary cirrhosis, the results have not been favorable. The course of the disease has been influenced little, if any, by the operation. In portal cirrhosis, on the other hand, a certain number of the patients showed definite improvement and Giffin concludes that when there is a long-standing, marked splenomegaly the patient may benefit from a splenectomy. The operation is not particularly serious if the time for its performance is well selected and the condition of the patient carefully prepared.

HEMOCHROMATOSIS

Bronzed diabetes, pigmentary cirrhosis of the liver or hemochromatosis, is a disturbance of metabolism characterized by bronzing of the skin, enlargement of the liver and usually diabetes. Pathologically there is found advanced cirrhosis of the liver, sclerosis of the pancreas and extensive deposition throughout the body of pigment, most of which is iron-containing. It is an uncommon disease, only 81 cases having been found in the literature and reported by Blanton and Healy in 1921. The most complete recent study of the condition was published by Sprunt in 1911. He reported extensive pathologic studies of 3 cases.

The liver is extensively enlarged and shows an advanced cirrhosis. The pancreas is usually sclerotic though the islands of Langerhans are rarely affected. The spleen is moderately enlarged, its average weight in 15 cases being 400 gm. (Blanton and Healy). It often shows a moderate increase in the connective tissue of the capsulotrabecular system, sometimes a diffuse increase in connective tissue. The most marked pathologic feature of the disease is the extensive deposition of

pigment throughout the body. This pigment is for the most part iron-containing hemosiderin, but there is also a smaller amount of a golden yellow pigment in which iron has not been demonstrated and which has been called hemofuscin. These pigments are found in large quantity especially in the secretory cells of the glandular organs, but also in the heart muscle, the interstitial tissue of the testicle and in connective tissue bands in the liver. The amount found in the spleen is small compared with that found in other organs.

The onset of the disease is often rather sudden, with weakness or the symptoms of a severe diabetes, polyuria and polydipsia. The pigmentation of the skin is a bronze or ocher color which, after its first appearance, increases rather rapidly. It is often more marked on the face and hands than elsewhere. Sprunt collected 63 cases of which 50 presented diabetes. The diabetic symptoms are usually severe and dominate the clinical picture. The patient usually dies with acidosis. One patient is said to have recovered, but the diagnosis was not established.

The blood findings are normal except for the sugar content which is high. It is noteworthy that no anemia develops in uncomplicated cases and the fragility of the erythrocytes is either normal or diminished. A study of the iron metabolism in a number of cases has shown that there is a definite retention of this element, although the amount found in the organs at autopsy is much larger than can be accounted for by the small daily retention demonstrated in these metabolism studies.

The etiology and pathogenesis of this condition are unknown. It occurs almost exclusively among men. The treatment is confined to dietetic measures and is without much effect. The splenomegaly is but moderate and constitutes an unimportant part of the disease. So far as we know, splenectomy has not been performed in this disease and it is not indicated. Recently, Mallory, Parker and Nye have obtained some results in animal experimentation that suggest some similarities between hemochromatosis and chronic copper poisoning.

BERIBERI

Beriberi, or kakke, is a chronic disease which is prevalent in Japan, China, the Malay peninsula and the Philippines. It is now quite generally believed to belong to the group of deficiency diseases or avitaminoses, although a small group of investigators still adhere to the theory of its infectious origin. It has been recognized in China and Japan for hundreds of years and its association with the use of polished rice has long been known. The deficiency theory was strengthened by the work of Funk and of Funk and MacCallum who produced an analogous condition in pigeons by restricting them to a diet of highly milled rice and then brought about a cure by the administration of an extract made from the rice polishings. At the present time it is thought that

the absence of vitamin B from the diet is the fundamental factor for the production of beriberi, but that certain other factors may be of importance in leading to the frank expression of the disease.

Beriberi occurs chiefly between the ages of sixteen and thirty, although no age is immune. It attacks chiefly the poorer classes whose diet is apt to be most restricted. It may be either acute or chronic, and is divided into the wet, dry and mixed forms. The wet form is characterized chiefly by the presence of edema in addition to many of the paralyses and atrophies which are said to be more characteristic of the dry type of the disease. In fact, a pure type is rather uncommon and the most frequent form of the condition is the mixed, in which are seen the symptoms of both the wet and dry types. The onset is usually gradual with weakness and stiffness in the legs and the later appearance of cardiac symptoms and edema. Anesthesias, paralyses and atrophy develop and a general anasarca may appear. Digestive disturbances are common and the patient often becomes markedly emaciated. The anemia is usually only moderate. Cardiac weakness progresses and not infrequently causes the death of the patient. Occasionally acute pernicious cases are seen in which the disease progresses rapidly, paralyses are extensive and death occurs in three or four weeks.

Pathologically, the most prominent lesions are those of peripheral neuritis with degeneration of the myelin sheaths of the nerves. Degenerations also are found in the posterior columns of the spinal cord. The heart muscle exhibits fragmentation and granular degeneration. Edema and effusions into the body cavities, especially the pericardium, are often prominent findings.

The spleen is usually slightly enlarged in beriberi, though often not sufficiently to permit recognition of the fact during life. Nishikawa gives average weights of from 133 to 260 gm., in comparison with the normal weight of the spleen in Japan where the range is from 80 to 120 gm. The lesion is essentially a chronic stasis with diminution of the pulp cells and slight increase in the reticulum.

There is no satisfactory treatment of the disease. Some favorable results have been obtained by the administration of the extract of rice polishings. The most effective measures have been those which prevented the development of the disease by a regulation of the diet. Where it has been possible to do this effectively, as in the Japanese army and navy, the incidence has been reduced to about 1/300 of its former figure. The splenomegaly is an unimportant incident in this disease and requires no special consideration or treatment.

SCHISTOSOMIASIS

Infestation with schistosomum has been described in two forms. *Schistosomum haematobium* (Bilharzia) is common in Africa, especially in Egypt and the Transvaal. The intermediate host and the method

of transmission are not known. The adult worms live in the portal vein and its tributaries. The eggs are found in the urine. Cystitis and hematuria are prominent symptoms and the ova may form the nuclei of bladder calculi.

Schistosomum japonicum is found chiefly in Japan, China and the Philippines and produces cachexia, eosinophilia and bloody stools. The adult worms are found in the smaller mesenteric blood-vessels, and the ova are excreted in the stools and can sometimes be demonstrated in the circulating blood.

Patients suffering from infestation with either of these parasites are prone to develop enlargement of the liver and spleen. The liver enlargement is due to cirrhosis, and the splenic lesion is believed to be secondary. With the establishment of the hepatic cirrhosis, the patients are prone to exhibit the symptoms of the advanced stage of this disease, that is, ascites, cachexia and gastro-intestinal disturbances.

Nishikawa has studied the spleen in a number of these cases and points out that the diagnosis between schistosomiasis and splenic anemia may be difficult. The average weight of the spleen is 992 gm. and has been reported as high as 2,675 gm. The shape of the organ is not disturbed. The capsule is thickened and there is often perisplenitis and adhesions. The trabeculae are increased in size and often show deposits of hemosiderin. The venous sinuses are widened.

Nishikawa is of the opinion that the lesion is essentially a chronic stasis, the degree depending upon the chronicity of the disease. But he points out that the spleen of pure chronic passive congestion is not as large as it is in schistosomiasis and that the picture is generally more like that found in cirrhosis of the liver, though occasionally it resembles splenic anemia. Ova may be found in the trabecular veins but are apparently not found in the pulp. He inoculated twelve dogs with this parasite and found in their spleens changes which were much the same as those found in man.

In Japanese schistosomiasis, the principal symptoms are said to be dysentery, progressive anemia and cirrhosis of the liver with ascites. The blood usually shows a moderate eosinophilia and a leukopenia.

Bilharziasis is a common infection in Egypt where, it has been recorded, 10 per cent of the hospital patients harbor this parasite. Bladder irritation and hematuria are the most frequent symptoms and stones often form. Pirie believes that it is a common cause of cirrhosis of the liver and describes it as being associated with carcinoma of the liver in about one fourth of the cases.

The diagnosis is established by the finding of the ova in either the bloody urine or in the blood and mucus from the rectum. They have occasionally been found in the circulating blood.

There is no proper treatment of the disease. No drug has been found which will kill the parasites in the blood. It is often very chronic and patients may harbor the parasite for years without suffering much

distress. It is conceivable that in selected cases, where the cirrhosis of the liver is the prominent feature and symptoms of portal obstruction are beginning to appear, removal of the spleen might bring relief to the portal circulation and result in some improvement of the patient's condition. It is evident, however, that splenectomy would have no beneficial effect upon the infection itself and we have been able to find no record of its having been performed in this disease.

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CHAPTER VII

SYPHILIS OF THE SPLEEN, TROPICAL SPLENOMEGALY, TUBERCULOSIS OF THE SPLEEN, HODGKIN'S DISEASE

SYPHILIS OF THE SPLEEN

The spleen is frequently involved in all stages of syphilis except the primary. The type of involvement varies with the age of the patient, the mode of infection and the stage of the disease. The need for special treatment directed to the spleen also varies and it will be clearer if each type is considered separately.

In congenital syphilis, the spleen is nearly always, extensively involved. It is large, hard, red brown and occasionally presents an exudate on the capsule. The follicles are small and reduced in number. Microscopically, there is round cell infiltration of the trabeculae and the vessel walls and a thickening of the reticulum of the pulp. There is a progressive cellular connective tissue growth which involves the whole stroma. The pulp is poor in cells and there may be brown granular pigment in the stroma. Occasionally one finds numerous miliary gummata, a lesion which is said to occur only in the congenital type of the disease. In the majority of instances, these patients respond well to treatment with arsphenamine.

In hereditary syphilis, the spleen is frequently involved, but not so often or to such an extent as in the congenital cases. When it is involved, it may be enormous in size and the associated symptoms present the picture of splenic anemia or of von Jaksch's anemia, depending somewhat upon the age of the patient. In infants, there is rather more apt to be evidence of abnormal reaction on the part of the hematopoietic system, and the general aspect of the condition resembles that seen in von Jaksch's type of anemia. In older children, a leukocytosis is less easily excited and the red cell producing organs have achieved a greater stability. The anemia in the older cases is more often merely secondary in type without the great number of abnormal cells that are found in infants. One finds in the spleen a diffuse fibrosis or interstitial splenitis. The walls of the arteries show a marked thickening and there is some proliferation of the sinus endothelium. It is claimed that true "fibroadenie" is not found in this disease. The progress of the condition resembles that of splenic anemia and Banti's syndrome appears if the patient is not properly treated.

The diagnosis is supported by the finding of a positive Wassermann reaction in the blood of the patient or his parents. The Wassermann reaction is positive in from 90 to 95 per cent of the cases of congenital and hereditary syphilis and has, therefore, an important place in its diagnosis. Vigorous treatment with mercury and arsphenamine brings about marked improvement in the great majority of cases of hereditary syphilis and it is usually unnecessary to consider any other form of treatment.

In the secondary stage of acquired syphilis, there is apt to be a moderate grade of splenomegaly. It is most frequent in those patients who have a febrile reaction or extensive cutaneous syphilids. The spleen is moderate in size and firm and gives rise to no symptoms. The lesion is a combination of congestion and hyperplasia of the pulp. With the subsidence of the symptoms of the secondary stage or their disappearance following treatment, the spleen returns to normal. There is no need for treatment directed against the splenomegaly.

In the tertiary stage of syphilis, the involvement of the spleen may be focal or diffuse. Rarely the lesion is gummatous, in which case the spleen is irregularly enlarged and its contour resembles that caused by a neoplasm or a cyst. Gummata in the spleen are often associated with similar lesions in the liver.

More frequently the lesion is diffuse. At times the spleen is apparently the only organ affected, but generally there is also a syphilitic cirrhosis of the liver (*hepar lobatum*) and sometimes many of the other organs show evidence of syphilitic infection. So far as we know, it must be recognized that syphilis may exist coincidentally with malaria, cirrhosis of the liver or splenic anemia and that the presence of these diseases may complicate the histologic picture.

In the diffuse involvement of the spleen in tertiary syphilis, the organ may be only slightly enlarged or it may be enormous. Perisplenitis is frequently found. There is an endothelial overgrowth of the intima of the arteries in general, while the arteries in the pulp, and later the larger arteries, show a thickening of their walls and a tendency to obliteration. The entire wall of the vessels is involved and there is often some perivascular round cell infiltration. The central arteries of the follicles may show hyaline degeneration and some periarterial fibrosis. The venous sinuses are dilated and there is proliferation of their endothelium. The pulp cells show moderate hyperplasia. The trabeculae and the reticulum fibers are the seat of fibroblastic proliferation and the eventual production of an excessive amount of connective tissue. This new connective tissue is at first cellular and later becomes more dense. The resultant lesion is thus a diffuse interstitial splenitis which is similar to that found in both cirrhosis of the liver and in splenic anemia (Banti's disease), but which is ordinarily not so intense. Some authors believe that Banti's disease is always syphilitic.

Symmers has described a distinctive form of massive splenomegaly

of which he has seen 6 cases, all in syphilitics. The spleen is reddish and leathery and contains a variable number of pinhead-sized areas with brownish centers, which correspond to sclerosis and mineralization of the smaller arteries. There are also present numerous small vessels, found to be venules, in or around which hyaline deposits have occurred, but which are immune from mineralization. The splenic substance is extensively replaced by the overgrowth of inflammatory connective tissue. All of these patients present other anatomical evidences of syphilis.

The *symptoms* produced by syphilis of the spleen vary. In many cases there are no symptoms until the spleen becomes large enough to cause trouble by its size alone. Often, however, there is a secondary anemia, usually of a moderate grade but occasionally severe. From time to time, one meets patients whose clinical condition simulates that of advanced cirrhosis of the liver or splenic anemia. They suffer with a secondary anemia, gastro-intestinal hemorrhages and a very large spleen. For one reason or another, the presence of syphilis is suspected and antisyphilitic treatment results in recovery.

The *diagnosis* of syphilis, whether of the spleen or of any organ, is closely related to a consideration of the significance of the Wassermann reaction. It is our opinion that the majority of the medical profession has too much confidence in the value of this test and in consequence has come to neglect that careful search of the history and of the patient for evidences of syphilitic infection which alone will bring successful diagnoses in many cases. A positive Wassermann reaction is one symptom, not necessarily pathognomonic, of syphilis and is absent in a large percentage of the cases of tertiary syphilis. When circumstances permit, the therapeutic test should be applied and the manner in which the patient reacts to one or more doses of arsphenamine may definitely determine the diagnosis.

When the diagnosis of syphilis has been made, the patient should be treated with arsphenamine and mercury. In a number of cases, perhaps the majority, this treatment will be followed by a disappearance of all symptoms and a subsidence of the spleen to its normal size. Sometimes the spleen remains moderately enlarged, but the patient appears to be cured. There are other patients with syphilis and splenomegaly, in whom, in spite of vigorous antisyphilitic treatment, the Wassermann reaction remains positive and who tend to develop various syphilitic manifestations as soon as the treatment is interrupted. It is believed that, in these cases, the spirochetes remain in the spleen protected against the action of the arsenic or mercury which the patient receives, by the dense fibrous tissue bands in that organ. From these hiding places they issue forth as soon as the blood is free from spirocheticidal drugs and renew their warfare against the body. When we find the latter condition present, the advisability of doing a splenectomy deserves consideration.

Coupland first performed splenectomy in a patient with syphilis, although the diagnosis was not made until the death of the patient two years later. Hartwell, in 1913, and French and Turner, in 1914, reported additional cases, and in 1916, Giffin reported 3 cases from the Mayo Clinic. In all of these 6 cases, the patient improved considerably after the operation. In 1921, Giffin reported 6 splenectomies for syphilis, with 1 death from hemorrhage. Out of Symmers' 6 cases, 4 which showed peculiar vascular changes were subjected to splenectomy, and 2 of them died after the operation. The rather frequent presence of adhesions increases the difficulty and consequently the mortality of the operation, but the mortality is apparently not greater than in splenectomy for other conditions.

The rationale of the operation is elusive. Several obvious possibilities suggest themselves. First, that spirochetes, harbored in the spleen in spite of treatment, continue their activity. This supposition is supported by the fact that Balfour found spirochetes in large numbers in the three spleens removed; also that the Wassermann reaction could be rendered negative only temporarily by medical treatment. Second, that the permanently diseased spleen causes a disturbance of the hematopoietic functions resulting in profound anemia and its attendant symptoms. Third, that the diseased spleen is responsible for toxins which are a cause of the anemia. Fourth, some observers believe that the disturbance is largely mechanical and the improvement due to removal of the large spleen. The first of these suppositions appears the most tenable.

Antisyphilitic treatment should be insisted upon for some time after the operation; in some of these cases the patients reacted to treatment much more favorably after the operation than before. In Coupland's case, the diagnosis was not made and yet the patient improved and lived for two years, dying eventually of portal obstruction. Patients with syphilitic splenomegaly should, therefore, have intensive treatment for a time. If the symptoms do not improve, splenectomy is indicated. Antiluetic treatment should be resumed after recovery from the operation.

TROPICAL SPLENOMEGALY

There are a number of diseases peculiar to tropical climates which are associated with enlargement of the spleen. Some of them are infectious diseases that have been carefully studied and are fairly well understood. With others, both the cause and the nature of the disease is unknown. This is due in part to the infrequency of the condition and in part to a lack of opportunity for careful study.

Malaria.—Malaria, in its acute form or even as a mildly chronic disease, is not uncommon in the northeastern part of the United States, but it reaches its greatest virulence and most persistent activity in the tropics and is properly classified as a tropical disease. It would be out

of place to present here a detailed description of malaria and we propose to limit ourselves to those elements of the disease which interest us in a study of the reaction of the spleen to malarial infection.

The disease as we see it here is a relatively benign infection due to a form of hemocytozoa, which yields readily when quinin is properly administered, though occasionally the more persistently chronic cases are imported from the tropics. It is usually acute. When not properly treated, mildly chronic cases occur. In the southern states, semitropical conditions obtain and the disease approaches in virulence the type seen in the tropical zone. Acute cases are much more severe and are often fatal. A cerebral form of the disease is not infrequent and, in addition, one often sees persistently chronic types which resist thorough treatment, produce a severe cachexia and are responsible for a large mortality.

The plasmodium, which is the cause of the disease, lives in or upon the erythrocytes and destroys them. As a direct result of this activity, the patient suffers from an anemia, and altered blood pigment collects in various organs of the body. At the same time, toxic materials are produced which cause other symptoms. The process is essentially the same regardless of which of the three forms of the parasite cause the infection. Only the details differ.

The spleen becomes palpable early in acute malaria but rarely reaches a large size. The average weight is about 300 to 500 gm. The lesion is an acute splenitis of the red type (see section on Pathology). The organ tends to lose its normal shape and to become globular. The capsule is thin and tense and the consistence is very soft. On section, the pulp bulges and is easily scraped away with the knife. It is sometimes almost diffuent. The follicles are large but are obscured by the bulging pulp. The trabeculae are not increased. On microscopic examination, there is seen an intense congestion with moderate hyperplasia of the pulp. Phagocytosis of the red cells is frequent and many cells contain altered blood pigment.

With recovery from the attack, the spleen returns to normal. The importance of the splenomegaly in acute malaria is found in the tendency of this soft mass to rupture upon the application of slight violence. Instances have been reported in which the trauma was so slight that the rupture has been called spontaneous. For this reason, the acute malarial spleen should be palpated with extreme gentleness and should never be subjected to puncture. Abscess of the spleen is a rare complication of malaria.

Acute malaria is one of the most frequent causes of rupture of the spleen, although Alport differs from most authorities, saying it is rare. When rupture does occur, the only treatment that deserves consideration is immediate splenectomy. A large number of such operations have been successfully performed. (*Cf.* Section on Rupture of the Spleen for a detailed discussion of this condition.)

In chronic malaria or malarial cachexia, as we see it in the vicinity of New York, the spleen is only moderately enlarged and does not of itself produce symptoms. In the tropics or in cases imported from there, the situation is very different. The spleen frequently weighs more than 1,000 gm. and Mourdas mentions one of 5,750 gm. With the repetition of acute attacks of the disease, there appear evidences of chronic splenitis. There is an increase in the fibrous tissue content and, at first, a hyperplasia of the pulp. Later the fibrosis predominates and the pulp cells are diminished by reason of the pressure of the increasing sclerosis. The lymphoid follicles are at first unaffected but later diminish and finally disappear. The normal shape of the organ is usually well preserved. It is hard and, on section, the cut surface has a grayish brown or blackish appearance due to the presence of large amounts of altered blood pigment. Perisplenitis is almost always present and adhesions are frequently found, especially at the upper pole. On microscopic examination, there is found the fibrosis and pulp changes mentioned above, and, in addition, a large amount of pigment in the macrophages and polynuclear cells and also lying free in the pulp. This pigment is melanin, and hemosiderin.

The diagnosis in acute malaria is readily made by the discovery of the parasite in the blood. In chronic malaria, the diagnosis can often be made only by inference. The most careful examination of the blood may fail to reveal the plasmodium. Anemia with a low color index, leukopenia with a relative lymphocytosis and the occurrence of basophilic stippling in the red cells is said to be strongly suggestive of lead poisoning or chronic malaria. The history of repeated attacks of malaria or of residence in a district known to be the location of much malarial infection may be the deciding point in the diagnosis.

The enormous spleen of chronic malaria may in itself be a cause of annoying symptoms. This is more apt to be the case when the organ is freely movable. When it is fixed in position by adhesions, it seems to interfere less with the other viscera. The patient complains of enlargement of the abdomen, dragging pains in the back and flank, disturbances of digestion probably due to pressure upon the stomach and duodenum, or interference with the progress of pregnancy. Any of these symptoms may be severe enough to require treatment.

Quinin is the specific remedy for malaria. It may be given by mouth, intramuscularly or intravenously, and, if given properly for a sufficient length of time, may cure the infection and lead to a regression of the spleen. Arsenic is occasionally helpful. But these methods do not always yield the desired results. The parasite either becomes resistant to or is protected against the action of the drug. Some authors recommend the application of X-rays to the spleen. It is said to be followed by improvement generally and at least one writer (Pentz) has reported an apparent cure following five such applications.

The enlargement of the spleen is but one of the evidences of

chronic malaria. The disease is not located exclusively in the spleen nor is that organ an incubator for the malarial parasite. Therefore the removal of the chronic malarial spleen will not bring about a cure of the infection. On the contrary, it may stir into activity an infection which had apparently been cured (Jiminez and Pittaluga). But parasites may remain in the spleen, protected against the action of drugs by the fibrous tissue barriers which result from the infection, and the removal of this focus may render the infection more susceptible to treatment. In addition, the large spleen may demand removal because of the symptoms it produces in a mechanical way.

The removal of the chronic malarial spleen is a serious operation. The adhesions which are usually present interfere with the rapid performance of the operation, and there are several reported cases in which splenectomy could be only partial because of them. Mourdas reports 20 splenectomies with a mortality of 40 per cent, and other authors report figures that show a mortality between that and 25 per cent. There is reason to believe that, with ideal conditions and careful preparation of the patient to subdue his infection, raise his hemoglobin and protect him against shock, this mortality might be effectively reduced. But splenectomy in chronic malaria will probably always be a serious operation. When successful, the results are usually good. The patient is relieved of the symptoms due to the large spleen and the vigorous prosecution of antimalarial treatment generally results in a cure of the infection.

Kala-azar.—Kala-azar, the "black sickness" or leishmaniasis, is a tropical disease due to infection with a protozoön, *Leishmania donovani*. It is a chronic affection, lasting for months, and is characterized by irregular fever, anemia, leukopenia, dark pigmentation of the skin which gives the disease its name, enlargement of the liver and spleen, and cachexia. The "tropical splenomegaly" of India, Indo-China and Ceylon is largely due to kala-azar. The parasite is occasionally found in the circulating blood, but is commonly located in the macrophage cells of the liver and spleen. It has been cultivated upon artificial media.

There are two forms of the disease. That known as kala-azar affects adults, is found chiefly in India, Ceylon, Syria and Indo-China and is believed to be transmitted by the bedbug. The variety known as infantile kala-azar is found only in children in the countries bordering on the Mediterranean. The parasite in this type is called *L. infantum* but is believed to be identical with the *L. donovani*. It is believed that infantile kala-azar is transmitted by the dog flea. Most of the instances of infantile splenic anemia observed near the Mediterranean are assumed to be leishmaniasis. A third form of the disease, called tropical sore or oriental boil, caused by *L. tropica* or *furunculosa*, apparently does not involve the spleen.

The spleen is regularly involved in leishmaniasis and may grow to tremendous proportions, especially in the infantile type which may

resemble von Jaksch's anemia. The lesion is said to be essentially a congestion (Kaufmann) without thickening of the trabeculae, but with some thickening of the reticulum of the periphery of the follicles. There is hyperplasia of the pulp. The macrophages contain the parasite. The spleen is smooth and firm and is usually free from perisplenitis.

The diagnosis is made by the discovery of the parasite in material obtained by puncture of the spleen. While this procedure is somewhat dangerous, it can generally be done without serious effects if care is taken. Rogers reports 166 cases and says the mortality should not be above 1 per cent. Knowles reports 135 cases without accident. The patient receives gr. xx of calcium chlorid on the evening before and two hours before the operation. The spleen is held firmly in place by an assistant while the puncture is being made, and the patient should remain quiet for at least one hour afterward. This is a much shorter time than is advised by American authorities, who recommend a rest of twenty-four hours. Rogers says that, of those cases of splenomegaly in which the parasite was not found, 93 per cent cleared up on the administration of quinin and were, therefore, presumably due to malaria. Splenic puncture should not be performed in the presence of ascites, severe anemia or hemorrhages.

An extreme leukopenia is characteristic of this infection, counts as low as 2,000 being not uncommon. The mononuclear cells, especially the endotheliocytes, are relatively increased.

Within the past few years, the treatment of kala-azar with injections of tartar emetic has attracted attention and is said to be quite effectual. Whether actual cures have been brought about by this agent is not clear. If the patient improves under the antimony treatment together with blood transfusion and general hygienic measures, and it appears that the splenic condition is not improved and if the liver is not enlarged, then good results may be expected from splenectomy. On the other hand, splenectomy is contra-indicated if the liver is large or if the patient fails to react well to transfusions and antimony (Johnstone). Although the patient may benefit from the operation, it is necessary to continue the administration of antimony and the treatment of the anemia for some time. Before the introduction of these therapeutic measures, the mortality of the disease is said to have been 80 per cent. No figures are available to show how much reduction there has been recently in this mortality, because an insufficient amount of time has elapsed to permit accurate conclusions. But apparently there has been a definite improvement in the results obtained by modern methods.

Relapsing Fever.—Relapsing fever represents a group of closely related infections caused by spirilla or spirochetes which differ in the different localities in which the disease is found. The organisms have been described by Obermeier, Novy, Carter and others. They are transmitted by ticks. The disease is characterized by paroxysms of fever which last five or six days and recur after intervals of about the same length of time.

The organisms can usually be found in the circulating blood during the early part of the febrile period.

During the febrile period, there is an enlargement of the spleen which is similar pathologically to that seen in other acute infections. The lesion is an acute splenitis of the red type and is marked by extreme congestion.

Treatment is best carried out with arsphenamine or neo-arsphenamin and the results are uniformly satisfactory. The spleen rapidly returns to normal with the disappearance of the infection, and there is no need for surgical interference.

Egyptian Splenomegaly.—Richards calls attention to a condition which has been called "endemic splenomegaly with cirrhosis" or "Egyptian splenomegaly." As he describes it, the condition appears to bear a striking resemblance to splenic anemia as it occurs in Banti's syndrome. There is splenomegaly, anemia, cirrhosis of the liver, leukopenia and ascites. Pathologically, he mentions dilatation of the venous sinuses, hyperplasia of the reticulum and a replacement fibrosis of the malpighian bodies. The spleen weighs from 535 gm. to 2,780 gm. It is often associated with Bilharzia or Ankylostoma infestation. Fever is not uncommon, but hematemesis is rare. Death occurs from exhaustion.

Malaria and kala-azar cannot be demonstrated in these patients. Richards is of the opinion that the condition is an infection and that the hepatic cirrhosis "is an essential part of the disease from the beginning."

He reports 22 splenectomies in this disease, with 4 deaths and 18 "recoveries," where patients have remained well for periods up to two and a half years. He says that splenectomy is not advisable after the development of ascites.

Colombian Spleen.—In Central America there is seen a form of chronic splenomegaly which has come to be known as "Colombian spleen" because it has been observed principally on the Isthmus of Panama in individuals coming from Colombia. It is a very large spleen which is not accompanied by symptoms except those produced mechanically. Pathologically it resembles the spleen of chronic malaria in every way, except that there is absence of pigment (Bates). Because of this fact and because all persons who have been observed with this condition have come from districts in which malaria is prevalent, it is believed to be malarial in nature even though parasites and pigment are absent.

Splenectomy has been performed upon a number of these patients for the relief of symptoms due to the large mass in the abdomen. The operation is not especially difficult and the results are said to be good.

TUBERCULOSIS OF THE SPLEEN

Dependent upon the lesions found in the spleen and elsewhere, tuberculosis of the spleen has been subdivided into two main groups which

are usually designated as primary and secondary tuberculosis of the organ. Secondary tuberculosis indicates concurrent involvement of the spleen in a more or less well-marked general tuberculous infection. In this case, the splenic involvement is coincident and subordinate.

Primary tuberculosis, on the other hand, signifies that the lesion in the spleen is the predominating and apparently controlling lesion. The term, however, is a misnomer, since almost all authorities agree that the spleen is not the primary focus. Thus Klotz, in discussing 12 cases of healed miliary tuberculosis of the spleen in which no other focus was found at autopsy in spite of careful search, states that there is no doubt that some unrecognized focus had existed near the point of entrance of the infection. Brüns, however, on the basis of his case, believes that primary tuberculosis of the spleen may occur. In order to conform to custom, we shall employ the term "primary" tuberculosis, recognizing, however, its limitations.

The splenic infection is hematogenic. In most cases, it is undoubtedly dependent upon a small focus elsewhere which may subsequently heal. But the splenic focus dominates the picture and apparently becomes, in its turn, the source of bacilli which are thence transmitted elsewhere, especially to the liver through the portal system.

The splenic lesion is, therefore, in the large proportion of cases neither a primary nor an isolated focus; it may, however, be the dominating focus, and as such is amenable to operative treatment. The so-called primary tuberculosis of the spleen is, therefore, a surgical condition and will be considered at some length.

Winternitz reviewed the subject of primary tuberculosis of the spleen. In presenting a collection of 51 reported cases, he states that some liberality is necessary in accepting some of them, but that the vast majority are definite instances of massive tuberculous involvement of the spleen without any marked involvement of other viscera. The salient features of his analysis of the 51 cases are as follows: most of the cases occurred in individuals between the ages of twenty and forty, but the lesion was noted in all decades, even in a child one year of age and in a man of eighty. Males and females were equally affected.

The size of the spleen varied considerably, the extremes of weight being 150 gm. (Lefas) and 3,780 gm. (Rendu and Widai). The average was between 1,000 and 2,000 gm.

The lesions found in the spleen are essentially the same as those encountered in secondary tuberculosis. As a result of the reaction to an acute infection, the organ is enlarged, congestion and hyperplasia occurring as in other infections, the degree being proportionate to the intensity and acuteness of the infection. Characteristic tuberculous lesions occur to a variable degree. The affected spleens present either diffuse miliary tubercles studding the surface and scattered through the organ, or conglomerate tubercles or caseous masses, often 7 or 8 cm. in diameter. In some cases these caseous masses become cystic, the

cysts being lined with caseous material; others show evidence of being partially or completely healed. The predominance of one type is dependent upon the intensity or chronicity of the infection. Especially in the advanced chronic cases with large caseous nodules, firm adhesions are frequently found between the enormous spleen and the diaphragm.

Tuberculous lesions were found in other organs in a considerable proportion of cases. This is of interest in view of the discussion as to the occurrence of so-called primary tuberculosis of the spleen. Winternitz found that in 80 per cent of the cases in which the liver was examined it showed tuberculosis. In 57 per cent of the cases in which the lymph-nodes were examined, tuberculous involvement was found; the nodes affected were the mesenteric, ten times, cervical, three times, bronchial, twice, and splenic, once. In 40 per cent, the lungs showed evidence of tuberculosis, 16 per cent presenting healed nodules and 24 per cent active processes. In 66 per cent of the cases, tuberculous lesions were found elsewhere. In only 1 case was the spleen exclusively involved; in 3 cases, the liver and spleen were the only tissues which showed evidence of tuberculosis.

Winternitz summarized the symptoms as follows:

The onset of the disease is characterized either by pain or tumor or both in the splenic region (over 70 per cent). In a few instances these symptoms are associated with gastric or respiratory disturbances, loss of weight, weakness or lassitude. These cases, as a rule, have a chronic course. In contrast to the above group there is another much smaller group in which the symptoms of onset are more striking and characteristic of an acute infectious process. These have the following symptoms: collapse, fever, chills, backache, etc., and run an acute course. There remains still another group in which the symptoms of onset and the course are intermediary between the above two groups.

The blood picture is not constant. A note on the blood was found in 26 of the case reports. It was normal 9 times (34.61 per cent), anemic 11 times (42.30 per cent), and polycythemia occurred 6 times (23.08 per cent). As a rule, the white blood-cells were not increased. The skin may be normal, pale, cyanosed, or icteric. Purpura or ecchymosis also may occur.

In 40 of the 51 instances, a note on the lungs was found. Of these 40, the clinical findings were negative in 20 instances (50 per cent). Physical signs or symptoms of slight pulmonary or pleural involvement were presented in 15 instances. Clinical evidence of extensive pulmonary involvement was present in 5 instances. The lymph-nodes were mentioned in 35 cases. They were normal in 29 instances (82.8 per cent). In 37 cases, the reports are complete enough to determine whether there was any definite tuberculous process elsewhere. In 18 of these (48.6 per cent), there was no clinical evidence of other involvement.

In 7 (18.9 per cent), the liver was enlarged; in 5 (13.5 per cent), there was ascites.

The duration of the disease varied widely. It was stated in 38 of the reports. In the large majority the course was chronic, the chief features being enlargement of the spleen and pain in the left hypochondrium. The shortest illness was seventeen days.

The diagnosis must be difficult in most cases. But the condition may be suggested by the clinical history of tuberculosis elsewhere, the localized symptoms referable to the splenic region, especially pain and splenomegaly. As Winternitz states, "while the presence of polycythemia or cyanosis may be a help in diagnosis, the fact that they may occur in other diseased conditions of the spleen and may be absent in massive tuberculosis of this organ, limits their value. Progressive leukopenia may occur as in our case. This, too, may be of aid in locating the disease in the spleen. The fever usually runs a septic course, but, as in the case of Palumbo, our own and others, it may be remittent in character. The tuberculin reaction has been used in so few cases that its value cannot be stated. It should be tried by all means, though in our case the Calmette reaction was negative."

Death invariably results if the spleen is not removed. Of these cases, 34 were discovered at autopsy, the remaining 17 at operation. Of the 17, 10 patients (58.8 per cent) recovered, 5 died and in 2 the result is not stated.

Treatment.—We must admit that a tuberculous process may occur in the spleen with scant involvement of other organs; and that the splenic focus may be a rich source of bacilli which may be continuously transmitted to the liver and elsewhere.

It is a generally recognized surgical practice that well-defined tuberculous lesions be removed by operation if this can be done without undue risk. While it is not supposed that all tuberculous tissue is removed, it has been found in practice advantageous to remove isolated foci of the disease. The processes of resistance are thus conserved and concentrated upon a less extensive infection. If it is obvious, then, that the spleen is actively involved and other tissues are relatively free from the disease, the organ should be removed when this can be done without undue danger to life.

As to the prognosis, nothing convincing has been presented. As stated, operative recovery may be expected. But the tables of analyzed cases and case reports do not present the late results. When one considers the frequency of recurrence, especially in the adult, after operations for all tuberculous lesions—for instance, epididymitis, lymphadenitis, osteomyelitis—the prognosis cannot, in the case of the spleen, seem very favorable. Yet the spleen offers this advantage, that general dissemination of the bacilli is checked or modified by the liver. But although a permanent cure cannot be anticipated in a large proportion of instances, all indications point to the performance of splenectomy in

appropriate and favorable cases. Definite splenic involvement with a reasonable degree of resistance on the part of the patient and only slight involvement elsewhere, especially of the lungs, should be the criteria.

The performance of splenectomy may be difficult on account of solid adhesions, and the operation has been abandoned in a number of instances, the operator limiting himself to an exploratory laparotomy. Quénu sutured the diseased spleen into the abdominal wound, and the patient recovered at the end of four months, after the pathologic tissue had gradually sloughed off. However, splenotomy should be avoided if possible on account of the inevitable persistent fistula.

Secondary tuberculosis of the spleen is comparatively common. Reinhold is authority for the statement that the statistics of the University of Kiel from 1873 to 1889 showed that the spleen was involved in 280 of 428 cases of tuberculosis in children (66.7 per cent) and in 160 of 836 cases in adults (19.1 per cent).

Manicatide, in 12 autopsies on tuberculous children, found involvement of the spleen in 10. Analyses of all autopsy statistics show a similar large percentage of involvement of the spleen in tuberculous individuals, especially children.

The pathological anatomy of secondary tuberculosis of the spleen has been described by Besançon and others. As the splenic lesions are secondary and incidental and not amenable to surgical treatment, the subject need not be dwelt on in this article.

Healed Miliary Tubercles of the Spleen.—This lesion is of interest to the surgeon primarily in offering an explanation of certain opacities which at times are seen in the roentgenogram in the splenic shadow. They also illustrate the resistance which the spleen may offer to tuberculous infection.

Klotz has analyzed the subject at some length. His studies are based on autopsy observations, which included 172 cases of tuberculosis of which 69 showed involvement of the spleen. Of these, there were 40 in which healed tuberculous lesions were found. In the majority of cases, old tuberculous lesions were found elsewhere; but in 12 cases, no other lesions were recognizable. Few of the cases showed clinical evidence of tuberculosis. The nodules in the spleen were small, sharply defined yellow concretions, usually the size of a mustard seed, but occasionally larger, up to 0.75 cm. in diameter. The number varied from one to many. The outer coats consisted of fibrous tissue; the centers, in general, were fibrosed or calcareous. No tubercle bacilli were found in the many sections examined. The presence of these foci had no marked effect upon the uninvolved portions of the spleen, though some presented fibrosis and some adhesions.

It is unfortunate that bacilli could not be demonstrated in some of the cases in order to establish beyond question the tuberculous character of these lesions. It is likewise unfortunate that X-ray studies

were not made. Further observations on this subject may be found in Chapter III.

HODGKIN'S DISEASE

In 1832, Hodgkin described a number of cases of chronic enlargement of the lymph-nodes, among which were several instances of the disease which later came to bear his name. But it was not until the studies of Sternberg appeared that the pathologic histology of the condition was well described. The later contributions of Reed and Longcope aided in clarifying the situation and in describing the characteristic histologic changes.

Hodgkin's disease is a chronic disease, characterized by progressive enlargement of the lymph-nodes, usually associated with splenomegaly, anemia and symptoms due to the pressure of the enlarged nodes upon other organs. It is always fatal. It has also been called malignant granuloma and lymphogranulomatosis.

The nature of the disease is unknown. Although it was at first considered to be a form of pseudoleukemia, when its pathologic histology became better known it was recognized as belonging to the granulomata. The cause is believed to be some infectious agent. Up to the present time, no bacterial cause has been satisfactorily demonstrated. Sternberg was of the opinion that it was a peculiar form of the reaction of the lymph-nodes to tuberculosis. In 15 out of 18 cases which he studied, he was able to demonstrate the presence of the tubercle bacillus either by staining reactions or by animal inoculation. Later, when other investigators were unable to obtain such uniform results, the "Much granules" were described and it was thought that they might be the form in which the tubercle bacillus existed when it caused Hodgkin's disease. These organisms are antiformin-fast, but not acid-fast, granular bacilli which produce tuberculous lesions when injected into animals.

There is no doubt that tuberculosis and Hodgkin's disease may coexist in the same patient, but the present tendency is to explain this as a complicating, often a terminal, infection. In the majority of instances, it has been impossible to demonstrate tubercle bacilli in tissue from Hodgkin's disease or to produce tuberculosis in susceptible animals by inoculation of material from this disease. The suggestion that the infection might be caused by the bovine type of tubercle bacillus has not been supported by animal experimentation. The tendency now seems to be toward the belief that the tubercle bacillus is not the infecting agent in Hodgkin's disease.

In more recent times, there has been described a bacterium which has been almost a constant finding in the nodes in Hodgkin's disease. It is a member of the diphtheroid group of organisms and was named *Corynebacterium granulomatis maligni* by de Negri and Mieremet. Bunting

and Yates have been enthusiastic supporters of the theory that this bacillus is the cause of Hodgkin's disease and Billings and Rosenow claim to have had excellent results from treating patients with a vaccine made from the organism. Later, the same or a very similar organism was isolated from the lymph-nodes or spleen, not only in lymphosarcoma, pernicious anemia, leukemia, chronic arthritis and other diseases, but also in healthy nodes. In his argument, Yates groups together Hodgkin's disease, leukemia, lymphosarcoma, Banti's disease, etc., and says they may all be closely related in their nature and origin. He explains the findings in healthy nodes with the statement, "many are infected but few are susceptible." He claims that the injection of dead cultures of this organism into man results in early focal lesions and a typical blood picture, while the inoculation of living bacilli into animals produces an acute disease similar to Hodgkin's disease.

On the other hand, many see in the frequent finding of this organism in various lesions, an indication of the absence of any pathogenic relationship to Hodgkin's disease or, indeed, to any of the other conditions. Furthermore, many types of bacteria have been found in the lymph-nodes and spleen of Hodgkin's disease. Immunological studies carried out with the diphtheroid and the blood of patients suffering with Hodgkin's disease have failed to yield results that would indicate a pathogenic relationship of the bacteria to the disease. In consequence, there are comparatively few at the present time who believe that Hodgkin's disease is due to an infection with this diphtheroid bacillus.

Still more recently, Kofoed, Boyers and Swezy have observed two patients in whom there existed both Hodgkin's disease and amebiasis. They have observed cells in tissue from other cases of Hodgkin's disease which they think resemble amebae and question whether in the *Ameba histolytica* may be found eventually the cause of this condition. It is as yet too early to form any opinion of this theory.

It has been suggested that Hodgkin's disease is neoplastic in nature. Instances have been described in which the masses of characteristic tissue were definitely infiltrating. There have been a few cases in which material excised from a patient at different times has been diagnosed Hodgkin's disease at first and lymphosarcoma later. There are seen occasionally specimens of lymph-nodes and spleens in which the diagnosis varies between Hodgkin's disease and lymphosarcoma and the histologic picture of the lesion presents a condition lying between the two. In typical Hodgkin's disease, the lesion is granulomatous in nature, shows fibrosis as the condition develops and has not the unrestricted growth seen in malignant neoplasms. In the majority of instances, the growth is well circumscribed and the near-by organs are affected by pressure only. The intermediate cases present a problem which has resisted solution.

Symmers has suggested that "Hodgkin's disease is primarily neither an infective nor a neoplastic lesion of the lymph-nodes, but a systemic

disease which expresses a predilection for lymphoid tissues, giving rise to multiple foci of growth at approximately the same time and in response to the same provocative agent." He has constructed an ingenious argument in support of his contention. He does not deny that the provocative agent may be a bacterium.

In a summary of these arguments, we are able to say only that in Hodgkin's disease we are dealing with a lesion that is apparently granulomatous but that the nature of the underlying infection is unknown. While the adherents of the tubercule bacillus and of the diphtheroid bacillus have some good arguments to support their theories, they have as yet been unable to demonstrate to the satisfaction of authorities generally that they are dealing with the true etiologic factor.

The earliest change in the lymph-nodes is a hyperplasia of lymphoid cells. Later the lymph-nodes lose their characteristic structure and the tissue is filled with closely packed cells among which certain particular varieties are present. A peculiar type of giant cell is probably the most characteristic. It is called the Sternberg or Dorothy Reed giant cell. It is large, usually multinucleated, but sometimes containing but one large nucleus. In distinction to the Langhans' giant cell, the nuclei are situated in the center of the cell. Eosinophile cells are frequent early in the disease but tend to disappear later. They are principally polynuclears, though myelocytes have been described. There are also seen large undifferentiated mononuclear cells that have been called endothelioid cells. Soon fibroblasts appear, the stroma proliferates and the organs show a fibrosis that may become extreme. The increase in connective tissue may interfere with circulation and result in necrosis. The nodes increase in size and become matted together in a mass of connective tissue, but the individual node remains discrete within its capsule.

The spleen is enlarged in the majority of cases. Occasionally it is very large. On microscopic examination, it shows the same picture as the lymph-nodes. Sometimes, in an advanced stage of the disease, the spleen is found to have undergone amyloid degeneration. Lymphoid tissue in the tonsils, intestines and elsewhere undergoes the same pathologic changes. The bone marrow shows a lymphoblastic reaction with proliferation of large mononuclear cells and also of eosinophils. Neighboring organs may be injured by the pressure of the growing masses of nodes.

Hodgkin's disease occurs more often in males than in females and usually in young adults. Infants have been known to be attacked. It is fairly frequently seen. The onset is insidious. It may be preceded by an attack of tonsillitis. The first symptom is usually the enlargement of one of the cervical lymph-nodes. This continues and other nodes in the group are involved until a large mass forms in the neck. The nodes in other regions are involved gradually, sometimes after long intervals. It is unusual for the primary involvement to take place

in other places than the neck. During this period, the general condition of the patient is good. Often the only complaint is that of the mass in the neck. As the disease progresses there may be attacks of fever. In one type of the disease, that which has been called Pel-Ebstein disease, there are periodic febrile periods lasting about ten days separated by afebrile periods of about the same length.

As the deep lymphatics become involved, there arise symptoms due to pressure upon important organs. The mediastinal nodes are practically always enlarged and cause cough, dyspnea and cyanosis. Pain is infrequent except as a pressure symptom. Bronzing of the skin has been described, and pruritus may be an annoying manifestation. In the terminal stages of the disease, there is marked emaciation and asthenia. Anasarca may develop and the patient dies from exhaustion, provided the course of the disease is not previously terminated by some intercurrent infection.

There has been a great deal of discussion concerning the blood picture in Hodgkin's disease. Bunting claims that he is able to make a highly probable diagnosis merely by the examination of a stained blood smear. He describes a relative and absolute increase in the large mononuclear and transitional cells, the so-called endotheliocytes, an increase in the blood-platelets and the presence in the blood of detached pseudopodia of megakaryocytes. These cells are often increased, but other hematologists have not been as successful as Bunting in diagnosing the disease from the film.

Early in the disease there is no anemia. Later a secondary anemia appears, mild at first, but becoming more severe with time, and often extreme at the end. Nucleated red cells are not often found. The total number of white cells varies little from the normal, being sometimes moderately increased and again moderately decreased. An eosinophilia may be present at any stage of the disease but is not constant. Late in the disease, when fibrosis of the nodes has become extreme, there may be a marked diminution in the lymphocytes.

X-ray treatment may produce remarkable changes in the blood picture. One of our patients improved for a time under this form of treatment, then suddenly the leukocytes rose to about 75,000 and the film showed an extraordinary collection of pathologic leukocytes, both myelocytic and lymphocytic. Death occurred within a few weeks.

The spleen is usually palpable and may reach an enormous size. There have been reported a few instances in which the splenic enlargement has apparently been the only clinical evidence of the disease; while in some cases in which autopsy or operation was performed, the lesion in the spleen has appeared to be older than that in the lymph-nodes. In most of these cases, the evidence is not conclusive; though in Mellon's case it is quite suggestive. Theoretically, so far as we know, there is no fundamental reason why the lymphoid tissue of the spleen should not be affected before that of the lymph-nodes.

The course of the disease is usually chronic and averages about three years. An acute form is described and Osler mentions a case in which the whole course was less than ten weeks. At times, the duration is indefinitely prolonged and the changes may be apparently restricted to the original swelling in the cervical nodes for several years before other groups of nodes are involved.

The diagnosis is made most satisfactorily by the excision and microscopic examination of one of the superficial nodes. Early tuberculous cervical lymphadenitis may be difficult to differentiate without this procedure. Later tuberculous lesions are usually readily diagnosed. The use of tuberculin may be helpful. Tuberculous nodes generally coalesce, soften and form sinuses. Leukemia can generally be recognized by the blood picture. In an aleukemic stage, reliance must be placed upon the examination of a node. If primary splenic Hodgkin's disease occurs, its differentiation from splenic anemia is probably impossible except by operation.

There is no satisfactory treatment for Hodgkin's disease. Arsenic has been given for years and may be of some little benefit to the patient. All discoverable foci of infection should be eradicated whenever possible. The tonsils are especially blamed and may be removed or subjected to treatment with the X-ray. If in any case it should prove possible to remove all of the affected tissue, as when the process is limited to a single group of cervical nodes or in the earliest stage of "primary splenic Hodgkin's" disease, the operation might result in the cure of the patient. This is based upon the assumption that the infective agent is present only in those nodes or organs which show histologic changes, an assumption that lacks convincing evidence in its support. Unfortunately the majority of instances of Hodgkin's disease which come to the observation of the surgeon have progressed beyond the stage in which such complete extirpation of the diseased tissue is possible. X-ray treatment should be applied after the operation. We know of no cures that have been obtained in this disease, though Yates says that some apparent cures have been seen. The large spleen and masses of lymph-nodes subside rapidly under Roentgen-ray therapy but soon recur. Prolonged application of this treatment may be followed by serious breakdown in the hematopoietic system. There is no doubt that early and thorough removal of diseased tissue often results in a definite prolongation of the life of the patient. Radium has been used, but Yates claims that the results obtained by the X-ray are better. He also feels that some benefit is derived from the use of an immune serum produced with the aid of his diphtheroid bacillus. Vaccines made from this organism were for a time thought to be of help, but their use has been practically discontinued.

Splenectomy would be indicated in "primary splenic Hodgkin's" disease if the diagnosis could be made, but we know of no instances in which the operation has been performed. Careful search must be made for

involvement of the lymph-nodes, both by means of the X-ray and at the time of operation. Cases should not be reported as "cured" within three or four years after the operation, and after that period only cautiously. Splenectomy may also be indicated for the relief of symptoms produced mechanically by the large mass in the abdomen.

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CHAPTER VIII

SPLENOMEGALY ASSOCIATED WITH DISEASES OF THE BLOOD: CHRONIC SECONDARY ANEMIA, VON JAKSCH'S ANEMIA AND SPLENIC ANEMIA (INCLUDING BANTY'S DISEASE)

CHRONIC SECONDARY ANEMIA

Chronic secondary anemia, or simple anemia, is a symptom, not a disease. As its name implies, it is always secondary to some other condition. It, therefore, deserves consideration only because it may be accompanied by splenomegaly and, when such is the case, the problem of differential diagnosis may be difficult.

Etiology.—Chronic secondary anemia may be due to impaired nutrition, such as may develop in the presence of chronic disease of the gastro-intestinal tract, or in prolonged lactation, or in the advanced stages of malignant growths. It may follow repeated hemorrhages or be due to the activity of intestinal parasites. It may follow acute or chronic infections such as typhoid fever, tuberculosis or malaria, or be one of the effects of intoxications as by lead, anilin or nitrobenzol.

When an enlarged spleen accompanies a secondary anemia, the pathologic changes found in that organ are characteristic rather of the cause of the anemia than of the anemia itself. Thus, in nitrobenzol poisoning, the splenomegaly is of the spodogenous type, due to the fact that the spleen handles a greatly increased number of disintegrating erythrocytes. In chronic malaria, recurring attacks of acute splenitis result in a permanent splenomegaly characterized by fibrosis.

The symptoms of secondary anemia *per se* are pallor of the skin and mucous membranes, weakness, fainting attacks, dyspnea, indigestion, rapid pulse, cardiac murmurs and dilatation, albuminuria and fatty degeneration of the viscera. In the majority of cases the blood shows a diminution in the red cell and hemoglobin content, the latter to a greater extent than the former. In consequence the color index is low, usually from 0.6 to 0.8. The red cell count rarely reaches such low figures as are frequently noted in some of the primary anemias. The red cells are well formed and regular in size but show more or less central pallor depending upon the severity of the anemia. Nucleated red cells of the normoblastic type are frequently present and with them there is generally a certain amount of polychromatophilia. This is the blood picture which has come to be considered as characteristic of secondary

anemia. The leukocytes may or may not be affected, depending upon the exciting cause of the anemia.

In some cases of anemia secondary to carcinoma of the stomach, infestation with the *Bothriocephalus latus* and rarely following repeated hemorrhages (Butterfield and Stillman), one may find a blood picture which can be differentiated only with great difficulty if at all from that usually seen in pernicious anemia. The red cells are reduced proportionately more than the hemoglobin so that the color index is greater than 1.0, and the more atypical forms are found. Poikilocytosis and anisocytosis may be marked and megaloblasts may be present. The diagnosis depends in these cases upon the demonstration of the parasite or the carcinoma or perhaps upon the findings at autopsy.

Thus, in any case of anemia, it often becomes necessary to detect its underlying cause before venturing a diagnosis. The detection of such a cause immediately removes a case from the groups of primary and splenic anemias.

The treatment of secondary anemia is directed first toward the removal or cure of the cause of the condition and second toward the relief of the anemia itself. Splenic surgery has no place in the treatment of the anemia itself. Those primary conditions, which result in secondary anemia and in which the surgery of the spleen merits consideration, are considered elsewhere in this paper.

VON JAKSCH'S ANEMIA

(Anemia splenica infantum: Anemia pseudoleukemica infantum: Splenic anemia with leukocytosis in children)

Von Jaksch's anemia is a condition occurring in children and marked by anemia, slight enlargement of the liver and marked enlargement of the spleen and sometimes an enlargement of the superficial lymph-nodes. The blood picture is characterized by a well-marked diminution in the number of the red cells and the hemoglobin and a persistent leukocytosis of varying degree. The literature of splenomegaly with anemia in children dates back to Gretsels report in 1866, but it was in 1890 that von Jaksch first described the symptom complex which has come to bear his name. The nature of the condition is obscure, though the majority of investigators are fairly in accord with the idea that it is more closely related to the secondary anemias than to the primary group and that it represents rather a characteristic response of the infantile hematopoietic system to injurious stimuli than a distinct and independent disease.

Von Jaksch recognized the importance of rickets and syphilis in the etiology of this disease and since his time tuberculosis, gastro-intestinal disturbances, bronchopneumonia and malaria have been credited with etiological significance. Occasionally one meets with an instance of

this disease in which it is not possible to discover any underlying factor which may plausibly be blamed, but as a rule the patients show some definite condition which may be considered influential.

Most frequently the prominent underlying condition is rickets, and Marfan goes so far as to claim that von Jaksch's anemia and rickets are identical. According to his theory, the primary lesion in rickets is a change in the bone marrow and a consequent compression of the osteogenetic portion of the bone. In those instances of von Jaksch's anemia in which there are no evident signs of rickets, he argues that this disturbance of bone formation has not occurred. The theory is interesting but it has not yet been possible to demonstrate its truth. It is well known that rickets is accompanied by an anemia which may be severe and by a splenomegaly, but the anemia is usually of the type of secondary anemia. From the time of von Jaksch, cases have been observed in which it has not been possible to detect any evidence of rickets and we are forced to regard Marfan's theory as unsupported by sufficient evidence.

Ward mentions the claim of Martelli that cases of von Jaksch's anemia are potentially leukemic, and that of Rivière, that the leukemia of children is merely a more advanced stage of this disease. Close relationship between leukemia and von Jaksch's anemia appears improbable in the light of our present conception of these conditions. The essential changes in the one appear to be in the erythropoietic system, in the other in the leukopoietic system and we still tend to draw a rather sharp line of distinction between the reactions of these two tissues.

The blood findings have led to the suggestion that von Jaksch's anemia represents a pernicious anemia in children, the differences from the classical picture in that disease being due to the different manner in which the hematopoietic organs of the child react to stimuli. The similarity of the two conditions cannot be denied, but the differences are no less distinct. The leukocytosis, the frequent low color index, the absence of achylia and of the neurologic findings that are so frequent in pernicious anemia, the better prognosis and better reaction to splenectomy are prominent features by which we feel justified in denying the identity of these two conditions.

Bartlett says, "Von Jaksch's disease is at present *sub judice*, being regarded by some as not a distinct entity." On the basis of the histologic pictures in the spleens in his cases, he states that it might well be a stage of Banti's disease. Apparently the reaction of the spleen is not characteristic in this disease. His pictures do not show the cellular hyperplasia and the compressed sinuses described by Stillman and seen in our cases, and yet clinically the patients appeared to be typical instances of von Jaksch's disease. There is no doubt of the similarity to Banti's disease shown by his illustrations, but they are quite different from the conditions we found in the spleen in our cases. But we must admit the possibility that it may some time be shown that von

Jaksch's anemia is merely the form which splenic anemia takes in children. It has been noted that the spleen readily becomes enlarged in many forms of anemia in childhood, possibly because it easily reverts to the embryonal erythropoietic function so recently lost, and some of the histologic evidence suggests that this reversion may, in fact, account in part for the splenomegaly. We agree with Giffin that the tendency in diagnosis should be away from splenic anemia whenever possible and to us it seems right to segregate under a separate name this group of cases which show a characteristic blood picture.

Hallez and Ward support the toxic-infectious theory of the disease. Ward views the condition as the reaction of the infantile blood-forming

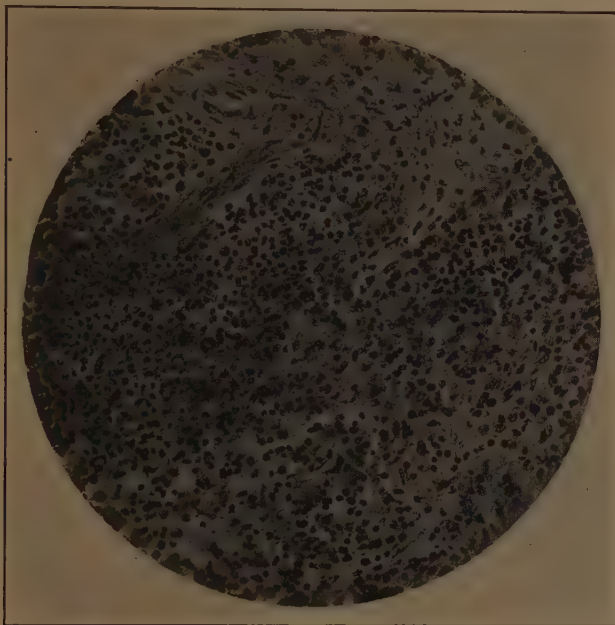


FIG. 31.—MICROPHOTOGRAPH OF SPLEEN. (From N. Y. H. Path., No. 18,199.)

Von Jaksch's anemia. The portion of the margin of the lymph follicle shows the irregularity so often seen in this disease, the effect of "compression." The hyperplasia of the pulp is also well shown.

organs to an infection, not necessarily a specific one, usually in the presence of rickets. He believes it might be appropriately called a secondary leukemia. Stillman, in 1917, after a study of the condition, concluded that "von Jaksch's anemia is due to the action of toxic or infectious agents which may or may not at the same time produce rickets. The source of these toxins is not necessarily in the gastrointestinal tract." Nothing in the evidence submitted since that time has led us to alter this conclusion.

Pathology.—There is anemia of the organs, often associated with more or less fatty degeneration. There may be petechiae and in some instances there have been described hydropic collections in the body

cavities. The lymph-nodes are apt to be enlarged and cherry red, the so-called hemolymph-nodes. The liver shows a reversion to the embryonal type of blood formation and exhibits areas of hematopoiesis. Cirrhosis has not been described. The bone marrow is dark bluish red and hyperplastic—of the myeloblastic type. Films made from these organs reveal the presence of nucleated red cells. The spleen is very large and varies in color, being bright red, dark brown and bluish gray in Stillman's cases. The consistence is tough and firm. The follicles appear small or absent. Microscopically, there is atrophy of the malpighian bodies, apparently due, in part at least, to compression by the hyperplastic pulp. The pulp shows an increase, chiefly in undifferen-

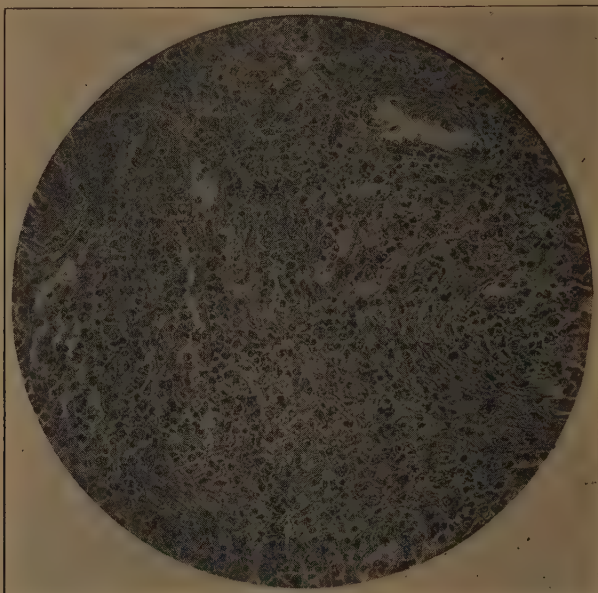


FIG. 32.—MICROPHOTOGRAPH OF SPLEEN. (From N. Y. H. Path., No. 17,233.)

Von Jaksch's anemia. The moderate increase in the fibrous tissue and the hyperplasia of the pulp can be seen.

tiated mononuclear cells and generally myeloid metaplasia. There is a diffuse connective tissue increase which varies in degree depending upon the age and severity of the disease.

The above findings in the spleen were constant in the three cases examined by Stillman and in one other which he mentions in a footnote. The question as to whether they may be considered as pathognomonic of von Jaksch's anemia is still open. Variations in the degree of the several elements which go to make up this picture are met in cases that do not conform clinically to the accepted type of the disease, and it is impossible to say how far the nature of these cases differs. It has been objected that one of Stillman's cases is not a true von Jaksch's anemia and, if that is so, we must assume that the pathologic

changes in the spleen as described above are not pathognomonic though they may be more or less characteristic. Nevertheless in the effort to avoid a diagnosis of splenic anemia, it is justifiable to collect under another title those cases which present certain factors in common, and in von Jaksch's anemia there are enough common factors to warrant separate consideration.

Symptoms.—Following the symptoms of the underlying disorder—rickets, syphilis, tuberculosis, gastro-intestinal disturbances, etc.—there gradually appear those of anemia in general. Pallor of the skin and mucous membranes, weakness and dyspnea are early symptoms. The heart may be enlarged and show a soft systolic murmur at the apex.

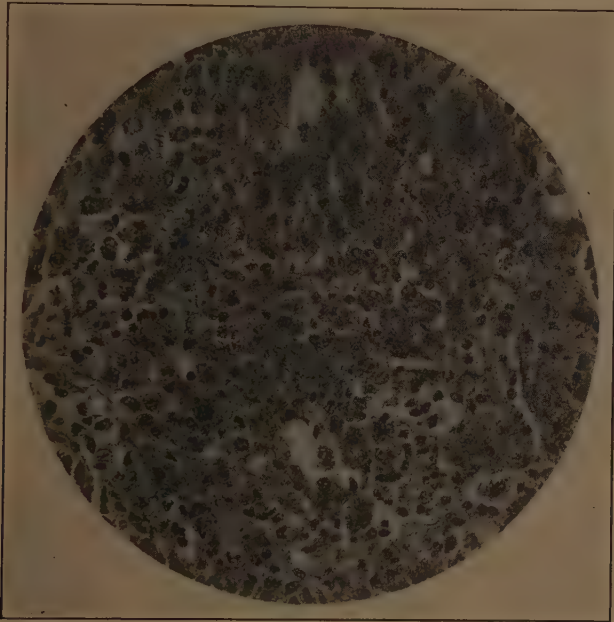


FIG. 33.—MICROPHOTOGRAPH OF SPLEEN. (From N. Y. H. Path., No. 17,233.)

Von Jaksch's anemia. In this higher power photograph it is possible to see the evidence of myeloid metaplasia. The large, dark cells are eosinophile myelocytes.

There may be a subcutaneous edema. The skin may have an icteric tint, but it is probable that true jaundice does not occur. There may be a moderate fever, but this is usually dependent upon the primary condition. Occasionally there is enlargement of the superficial lymph-nodes. The enlargement of the spleen appears early in the disease and may reach an extreme degree. It is firm, smooth and not tender. The enlargement of the liver appears later and is not so extreme.

The examination of the blood must determine the diagnosis. There is marked diminution in the hemoglobin and in the number of the red cells. The hemoglobin may be as low as 20 per cent and the red cells down to 1,000,000. The color index is usually less than 1.0, but may

be high. The range is usually between 0.6 and 1.1. Naegeli is responsible for the statement that the higher the color index, the worse the prognosis. The erythrocytes show an extreme departure from the normal. Anisocytosis, poikilocytosis, polychromatophilia and granular degeneration (basophilic stippling) are often marked, and erythroblasts may be very numerous. Both megaloblasts and normoblasts are often seen and attention has been called to a very early form of the megaloblast in which the cytoplasm is intensely polychromatophilic and contains little or no hemoglobin. The recognition of cells of the latter type is important because they are readily mistaken for lymphocytes. In those instances in which the color index is high, the blood film bears a striking resemblance to that seen in pernicious anemia during an erythroblastic crisis.

Leukocytosis is an important element in the blood picture. It is insisted upon by Naegeli and is agreed to by the later authors. It varies in degree in different cases and at different times in the same case. It may be as low as 10,000 and may reach 50,000. The differential count shows nothing remarkable. There is apt to be a lymphocytosis especially in young children, though occasionally the polynuclears predominate. The eosinophils are unchanged. Myelocytes, myeloblasts, plasma cells and Turck's stimulation forms are occasional findings.

Following the removal of the spleen in this disease, there is usually a tremendous increase in the number of nucleated red cells in the blood. This erythroblastosis may persist for a long period of time, as shown in one of our cases in which, seven years after the operation, there were still three or four nucleated red cells for each leukocyte. There is usually an increase in the leukocytosis immediately after the operation, but that gradually diminishes and reaches the ante-operation level or even normal in a few months. The blood changes are extraordinarily persistent even though the patient may appear to be cured.

The fragility of the red cells is normal as a rule. The observation of an increase in their resistance to hemolysis in one of our cases has led to a questioning of the diagnosis. The urine may show albumin and casts in small amounts. It frequently contains urobilin but rarely bilirubin.

Course and Prognosis.—The course is chronic. There is a gradual progression of the symptoms and, in the fatal cases, death occurs from weakness or from some intercurrent infection such as bronchopneumonia. When recovery takes place, there is just as gradual a disappearance of the symptoms, and the abnormal blood picture may be present long after the child is apparently well. It is said that most of the patients show a tendency to recover. Nevertheless an appreciable percentage of cases are fatal. The prognosis is better in the presence of some etiological factor that is amenable to treatment.

Differential Diagnosis.—The diagnosis must be made on the results

of the blood examination. The finding in a child of marked anemia with erythroblastosis and leukocytosis associated with splenomegaly strongly suggests the existence of von Jaksch's anemia. But the problem may be extremely difficult. This is well illustrated by a summary and further history of Stillman's 3 cases and the presentation of 2 other cases which have certain points of resemblance to the first 3.

Case I. M. M., aged nine years, was admitted to the First Medical Division of the New York Hospital on April 19, 1913. Family history negative. She gave no history of rickets but is said to have had malaria at the age of two and several times since, though the plasmodia had never been demonstrated in her blood. Her spleen had been large since the first attack of malaria.

On admission she exhibited pallor, weakness and retarded development. She was well nourished, her skin had a peculiar olive color and her heart was enlarged, presenting a blowing systolic murmur at the apex. The spleen was large, extending 14 cm. below the costal margin. It was hard, smooth and not tender. There were large, slightly tender nodes under the angle of the jaw.

Wassermann reaction was negative. The urine showed urobilin, but no bile. The red cells were 2,300,000, hemoglobin 25 per cent. Leukocytes 8,100 and polynuclears 58 per cent. The nucleated red cells numbered 4,300 per c.mm. A test of the fragility of the red cells showed that hemolysis began at 0.62 per cent NaCl and was complete at 0.44 per cent, so that the resistance was definitely diminished. "Vitaly stained" or reticulated cells made up about 35 per cent of the total number of red cells. Malarial plasmodia could not be found.

She ran a mild fever but improved gradually and was discharged after two months in the hospital with 3,900,000 red cells, 43 per cent hemoglobin and 13,500 leukocytes.

She did fairly well for a couple of months and then began to lose ground again. She was readmitted to the hospital on January 12, 1914, with 2,400,000 red cells, 25 per cent hemoglobin and 15,000 leukocytes. Nucleated red cells were present, but few. Her spleen was somewhat larger than before and her liver was palpated 10 cm. below the costal margin. She failed to improve under treatment and on March 21, 1914, her spleen was removed by Dr. Hitzrot. An accessory spleen was observed but not removed.

The spleen weighed 1,420 gm. and was surrounded by a number of adhesions. It was dark brown, firm and leathery and on microscopic examination showed atrophy of the follicles, hyperplasia of the pulp with a predominance of large undifferentiated mononuclear cells, marked myeloid metaplasia and considerable diffuse connective tissue increase.

Following the operation, she had a marked erythroblastic crisis, the nucleated red cells numbering more than 300,000 per c.mm. She con-

valesced rather slowly but satisfactorily and left the hospital about two months after her operation with a hemoglobin of 49 per cent and in good general condition. During the next three years she was seen at intervals and appeared to be in excellent health. She increased in weight, went regularly to school and progressed satisfactorily in her work. But her blood picture remained essentially unchanged. Her hemoglobin remained at between 50 and 60 per cent and there were constantly numerous nucleated red cells present. The leukocytes varied between 15,000 and 20,000.

During the latter part of 1917 and 1918, she suffered with comparatively mild attacks of phlebitis but was not seen by us. On March 15, 1920, she was admitted to the hospital with a temperature of 103° and acute pain in the lower abdomen. There was well-marked edema of the right leg and tenderness in the lower right side of the abdomen and in the groin. She passed through a severe attack of phlebitis in the right leg and right side of the pelvis and remained in the hospital for about two months. During the acute stage of the disease, the nucleated red cells almost disappeared from her blood. Her liver was still enlarged, the lower border being three fingers below the costal margin. She was definitely jaundiced and the urine contained both bile and urobilin. The resistance of the red cells had increased, for hemolysis was first apparent at 0.45 per cent NaCl and was not complete at 0.25 per cent. Leukocytes were 18,000, red cells 3,400,000 and hemoglobin 56 per cent.

She gradually recovered from this attack but found that her activity was limited by the swelling of her right leg, which was quite extreme and sometimes accompanied by pain. Her blood picture gradually returned to its previous condition. She was last seen seven years after her operation when she was fairly well except for her right leg. Her hemoglobin was 55 per cent and red cells 3,500,000, leukocytes 19,000 and erythroblasts 75,000. The red cells were still abnormal in size, shape and staining reaction.

The inclusion of this case with von Jaksch's anemia has aroused some discussion. Ward says that it is probably not one of von Jaksch's anemia, and Pearce, Krumbhaar and Frazier claim that it should more properly be classified as an instance of hemolytic icterus, chiefly because of the lessened resistance of the red cells to hemolysis and the increased percentage of reticulated erythrocytes.

In view of the almost uniform return to normal which follows splenectomy in hemolytic icterus, it does not seem proper to classify this case under that heading. It certainly shows the leukocytosis, erythroblastosis, anemia and splenomegaly that are considered characteristic of von Jaksch's anemia. But in addition the red cells presented an increased fragility. We have been unable to find in the literature the record of any instance in which such a marked erythroblastosis persisted for such a long time and in this respect we believe this case to be unique.

It may be that it does not represent a true von Jaksch's anemia, but we think it justifiable to classify it as such for the present.

Case II. S. K., aged eight months, was admitted to the New York Hospital on July 22, 1914. Family history negative. He was a premature child having been born at the seventh month of pregnancy. At two months he had bronchopneumonia. At four months, a second attack. At five months he began to suffer with gastro-enteritis and from that time failed to gain in weight, was restless and constipated. He was a poorly nourished, pale child with moderate signs of rickets. His spleen was enlarged, the edge being felt 6.5 cm. below the costal margin. Wassermann reaction negative. Red cells 1,400,000, hemoglobin 30 per cent, nucleated red cells 9,900, leukocytes 37,000, polynuclears 33 per cent. Under treatment he improved slightly and on August 17, 1914, his spleen was removed by Pool. The splenectomy was preceded by a transfusion.

The spleen weighed 105 gm. was smooth and bluish gray and firm. The cut surface was smooth, pale and grayish red. The malpighian bodies were few in number, extremely small and indistinct and the trabeculae were not prominent. On microscopic examination the follicles were small, the lymphatic elements evidently regressing. "The pulp is hyperplastic, the undifferentiated mononuclear cells predominating and arranged in cords and strands so that they form a network through the whole pulp. Myeloid metaplasia of the pulp is well marked. There is very little fibrosis."

Following the operation the red cells rose to 4,000,000 and hemoglobin to 85 per cent. The nucleated red cells increased at first until they numbered 131 for every 100 leukocytes, but soon fell until there were very few seen. The boy remained in the hospital for about two and one half months after his operation and when discharged was distinctly improved. Two months after his discharge he developed another attack of bronchopneumonia and died. No autopsy was obtained.

This patient presents a typical instance of von Jaksch's anemia which improved to some extent after the removal of his spleen, but he did not develop sufficient vitality to withstand an attack of bronchopneumonia coming four months after the operation. It must be considered as an instance in which the treatment was unsuccessful.

Case III. A. A., aged eighteen months, was admitted to the New York Hospital on April 14, 1915. Family history negative. She had cut her first teeth at the age of twelve months. She had not talked or walked up to the time of admission. Her abdomen had been noticeably large for about eight months. Two months before her admission she had had an attack of pneumonia.

On examination, a rachitic rosary was detected. The abdomen was large, the swelling being due in large part to the presence of a spleen which reached 15 cm. below the costal margin. It was hard, firm, smooth and not tender. There were a few discrete, enlarged nodes

in the submaxillary, anterior and posterior cervical chains and in the axillary and inguinal regions. The edge of the liver was felt 4 cm. below the costal margin. The Wassermann reaction was negative. Red cells were 2,700,000, hemoglobin 45 per cent, color index 0.8. Nucleated red cells numbered 1,400, leukocytes 12,000 and polynuclears 47 per cent. The erythrocytes showed marked abnormality in size, shape and staining reaction. On May 1, 1915, Pool removed her spleen.

The spleen weighed 227 gm. It was bright red, the capsule thin and the consistence rather tough and leathery. On section the cut surface



FIG. 34.—FIFTEEN MONTHS AFTER SPLENECTOMY FOR VON JAKSCH'S ANEMIA.



FIG. 35.—SAME PATIENT SIX YEARS AFTER SPLENECTOMY FOR VON JAKSCH'S ANEMIA.

was grayish red and finely granular. The follicles were numerous and fairly well circumscribed. The trabeculae were indistinct. On microscopic examination the pulp was found to be hyperplastic and to contain many minute hemorrhages and small collections of undifferentiated mononuclear cells. "Myeloid metaplasia is well marked. The follicles are compressed and fibrosis is slight."

Following the operation, this patient had the same erythroblastic crisis as the previous two. But a few days later she contracted measles which temporarily interrupted her convalescence. In spite of this mishap she was discharged six weeks after her operation with a red cell

count of 4,500,000 and a hemoglobin of 60 per cent. Her improvement progressed steadily though she did not talk or walk until she was more than two years old.

She was last seen six and one half years after her operation and at that time was said to be quite well except for an impetigo on her face. She nevertheless appeared to be underdeveloped for her age. Her blood count at that time showed 3,800,000 red cells and 85 per cent hemoglobin. Leukocytes were 10,400 and polynuclears 35 per cent. There were no abnormal red cells seen.

The patient represents a mild form of the condition, which showed a complete cure following removal of the spleen. It is not known how much the operation had to do with this result, but it can be said that improvement began only after the splenectomy. In spite of the apparent cure of her anemia, this patient still appears underdeveloped and of poor resistance, though her mother insists that she is quite well and is in the same class in school as other girls of her age.

The following two cases occurred in brothers. It is of interest to note that a half sister of these two boys, a girl whose mother was a sister of the mother of the boys, is said to suffer with a similar condition. The girl is older than the boys and is still in Italy.

Case IV. Alvaro B. was admitted to the hospital on March 18, 1920, when four years old. He was pale and had not grown well. His illness is said to have begun two years before with pain in the left side, a yellow color in the skin and a swelling of the abdomen. On examination he was pale, had large infected tonsils and carious teeth, his abdomen contained free fluid and his spleen was large. There was no evidence of rickets.

His Wassermann reaction was negative. The red cells were 1,700,000, hemoglobin 20 per cent, color index 0.58, leukocytes 9,000 and nucleated red cells many. The red cells showed the same marked abnormalities that were seen in the other cases. The urine showed urobilin but no bilirubin. The fragility of the red cells was slightly increased.

His spleen was removed by Dr. Hitzrot on April 16, 1920. It weighed 732 gm. Its color was normal, its capsule not thickened and the consistence increased. On section the cut surface was dark red and the malpighian bodies obscured. On microscopic examination there was an increase in the connective tissue, not diffuse but in strands around the minute vessels and as trabeculae. "Very few of the malpighian bodies resemble the normal. Lymphocytes are numerous but are present in small collections of apparently not more than ten or a dozen cells. There is hyperplasia of the pulp in which the large mononuclear cells are prominent. There is increased blood content and a large quantity of brown pigment granules. Very few myelocytes and nucleated red cells are seen." It is doubtful whether it can be said that there was any myeloid metaplasia in this spleen.

Following his operation he had the usual erythroblastic crisis, the nucleated red cells rising to 115,000, and there was a moderate leukocytosis, the white cells numbering 22,000. During his convalescence he passed through an attack of chicken-pox without much inconvenience. He improved gradually and not to a very great degree. His red cells rose to 3,600,000 and hemoglobin to 32 per cent and he gained in weight.

During the first few months after his operation, several teeth were removed and in December, 1920, he was again admitted to the hospital and a tonsillectomy performed. At this time his red cells were 2,000,000 and hemoglobin 32 per cent. Culture from the tonsils showed the presence of the *Streptococcus hemolyticus*. After the removal of his tonsils, his hemoglobin decreased slowly and in February, 1921, he received 265 c.c. of blood from his father. Following this procedure his hemoglobin rose to 55 per cent and his red cells to 3,500,000. At this time it was noted that his liver was enlarged. This improvement was only temporary for he returned to the hospital in September, 1921, seventeen months after his splenectomy with only 1,800,000 red cells, 32 per cent hemoglobin, 26,000 leukocytes and more than 100,000 nucleated red cells. At this time also he was definitely jaundiced and his urine showed a large amount of bile. The resistance of the red cells to hemolysis had increased for it was first noted in a concentration of 0.42 per cent NaCl and was not complete at 0.20 per cent. He died in the hospital in January, 1922, with pneumococcus meningitis. Autopsy was not obtained.

Case V. Armando B. was admitted to the hospital on the same day, March 18, 1920, when two years old. He had never walked. His illness began about one year before his admission, following an attack of persistent vomiting which had lasted for about three months. When examined he had a discharging left ear and an umbilical hernia. His spleen was large and his abdomen apparently contained free fluid. He was pale but his condition was apparently not so extreme as that of his brother. The red cells numbered 3,900,000 and hemoglobin 18 per cent. The leukocytes were 28,000, the nucleated red cells very few. The fragility was normal or slightly increased.

On May 5, 1920, he was transfused with 300 c.c. of blood and his spleen removed by Dr. Hitzrot. It weighed 490 gm. The capsule was smooth and not thickened, the color red and the consistence firm. Microscopic examination showed a reduction in the number of the follicles and a diminution in their lymphoid tissue content. The germinal centers were large when present but were not constant. There was hyperplasia of the pulp and some strands of new connective tissue. Nucleated red cells were found but myeloid metaplasia was doubtful.

On the second day after operation, his leukocytes were 75,000 and his nucleated red cells 324,000. This reaction soon became slightly less intense but was persistent so that one month after operation the leuko-

cytes were 29,000 and the erythroblasts 163,000. In the stained film the red cells showed the same marked abnormalities in size, shape and staining reaction that were noted in the previous cases. It was of interest to note in the study of these films that as long as one month after the operation it was possible to recognize red cells that, because of their normal size, shape and color were thought to be those which the child had received by way of transfusion.

In December, 1920, his tonsils were removed and he received 150 c.c. of blood transfused from his mother. At that time his leukocytes were 62,000 and his nucleated red cells 198,000. In March, 1921, he received a third transfusion of 240 c.c. of blood but with not very permanent benefit although he was discharged from the hospital two weeks later with a hemoglobin of 50 per cent. The other findings of the blood examination remained much the same as upon previous examinations. When seen in September, 1921, sixteen months after his splenectomy and three years old, he appeared to have improved more than his brother. His color was better and he had developed better. In December, 1922, he returned to the hospital for transfusion. His blood picture was practically unchanged and he had been losing ground for several months.

The diagnosis in the last two cases is puzzling. They present many points of similarity to Case I, and, on the basis of the leukocytosis, erythroblastosis, anemia and splenomegaly, they might be included with the cases of von Jaksch's anemia. The slight increase in the fragility of the red cells is like that shown in Case I, but the histologic picture presented by the spleen differed chiefly in the absence of any satisfactory evidence of myeloid metaplasia. In all five of these cases, erythroblasts appeared in the blood in large numbers after the removal of the spleen; but in Cases I, IV and V, they have persisted for a very long time, seven years in Case I. If we accept the idea that von Jaksch's anemia represents a characteristic response of the infantile hematopoietic system to injurious (toxic-infectious) stimuli, rather than a distinct and independent disease, it is not difficult to reason that the above five cases present merely individual differences in the reaction to stimuli that are conceivably not identical. The principal objection to such a course is that, if one admits first one variant of the classic type of von Jaksch's anemia and then two or perhaps three, one will soon be placing in this group cases that bear little or no resemblance to those originally described. These cases all correspond clinically to the picture described as von Jaksch's anemia and we feel that the opportunity to group them under a different title should not be lost. The name of von Jaksch's anemia should therefore be retained.

Treatment.—The treatment should be directed first against any etiological factors which may be apparent and which are amenable to treatment. Syphilis should receive vigorous treatment, and patients in whom syphilis can be recognized are apt to do very well under proper

therapeutic measures. All recognizable foci of infection should be cleaned up. Teeth and tonsils are the most frequent locations of these foci. Rickets and tuberculosis should receive such treatment as may be indicated. The child should receive wholesome food, and care must be taken to keep the digestive tract in as good condition as possible. Attention must be paid to the general hygiene. Sometimes a change to a more favorable climate is of benefit.

Those drugs are administered which have acquired a reputation in the treatment of anemia. Iron and arsenic are generally used and may be given in various forms. It is doubtful whether the organic compounds have any superiority over the inorganic preparations. Intravenous administration should not be necessary. Drug treatment of the anemia has probably little beneficial effect. Thorium X and the Roentgen ray have been used in a few cases, but their value is problematic.

The transfusion of whole blood is an important therapeutic measure in this disease. It benefits the patient in two ways: it relieves the anemia, at least temporarily, and is generally followed by an increased activity on the part of the hematopoietic organs. We know of no instances in which this disease has been treated over a long period with a series of blood transfusions before a splenectomy, but we believe that such a procedure might produce good results.

Giffin makes the statement that "in all diseases with splenomegaly and secondary anemia, the anemia is less severe after splenectomy than before even though the disease is not cured." On such empiric foundation is based the modern practice of treating so many types of splenomegaly with anemia by removing the spleen. In von Jaksch's anemia, the spleen takes an active part in blood regeneration and there is no evidence that it is pathologically active in blood destruction. Nevertheless splenectomy is indicated if the child shows no tendency to recover after a fair trial of medical treatment or transfusions.

A complete record of the splenectomies which have been performed for this condition is impossible since many of them are reported as cases of splenic anemia and there is frequently insufficient information to permit of a determination whether the case may be considered as one of von Jaksch's anemia. The operation is not a dangerous one, for, in 1917, Stillman was able to collect six instances without an operative death and in a footnote mentions a seventh. In 1921, Mayo said that they had removed eight spleens in such children without an operative death. Less is known concerning the later results. Clinical improvement appears early, but abnormalities in the blood picture may persist for years. Wolff's case showed a leukocytosis of 20,000 three years after operation. Stillman's Case I presents a blood picture seven years after operation that is in no respect better than that before the splenectomy. Stillman's Case II and d'Espine's case died of pneumonia within a few months after operation. Case IV died of pneumococcus meningitis twenty-one months after operation. Case V, two and a half years

after operation, shows only moderate improvement. Mayo says that "when the condition has not been too advanced cure has followed." This is probably a correct statement, though it may be difficult to determine whether the condition is too advanced. In no instance is it reported that the patient suffered harm as a result of splenectomy, so that every patient with von Jaksch's anemia who fails to improve with other treatment is entitled to this operation. Transfusion is an important adjunct to the operation.

SPLENIC ANEMIA

(Including Banti's Disease)

History.—The association of anemia and splenomegaly has been observed for many years although the term splenic anemia or anemia megalosplenica apparently was not applied to the condition until the publication of Gretsels's paper in 1866. Originally the diagnosis undoubtedly included a number of conditions which are now believed to be without relation to each other and some of these have been separated from the group as a result of clinical and pathological investigations in which were utilized the newer pathological and hematological methods as they were introduced. Although leukemia had been described before this time, it is probable that occasional instances were included with the splenic anemias until blood examinations became more frequent. When it was possible to show that some of the cases were due to malaria or to syphilis, they were excluded from the group. As pernicious anemia was more thoroughly studied, it was found that it sometimes simulated splenic anemia. Acholuric or hemolytic icterus and Gaucher's disease were studied with sufficient care to demonstrate that they deserved acceptance as independent clinical entities. In this way the group of the splenic anemias has gradually been diminished in size, and the definition of the condition has become rather more restricted in its significance.

But this process of partition has not been completed. The term von Jaksch's anemia has been applied to one group of cases even though a number of investigators still believe that it is merely the form in which splenic anemia may manifest itself in childhood. We have discussed this question in the section on von Jaksch's anemia and have there presented our reasons for believing that this condition is entitled to its own name. It is reasonable to expect that this group of splenic anemia will be still further reduced in size as newer methods of study are introduced and as our information increases. In fact it is not impossible that the term may eventually disappear completely.

In 1883, Banti described a condition with which his name has become associated, and has elaborated that description in more recent publications. This condition is characterized by unknown etiology,

chronic course, secondary anemia, a tendency to hemorrhage, a peculiar fibrosis of the spleen and the late development of cirrhosis of the liver of the Laennec type and ascites. Whether Banti's disease when fully developed represents a late stage of an ordinary splenic anemia or is an independent clinical entity is still a matter of dispute. When a case of splenic anemia goes on to the development of hepatic cirrhosis and ascites, it is easy to say that it has been really Banti's disease from the beginning. It is quite generally admitted that in their early stages the two conditions are indistinguishable. But it is unusual for a physician to be able to follow a patient throughout the full course of splenic anemia. It lasts for so many years and the medical treatment is so unsatisfactory and the disease is so frequently terminated by some intercurrent infection or a severe hemorrhage that the usual instance is observed by any one physician for only a comparatively short period. Therefore it is not known how large a percentage of cases, originally presenting the clinical picture of splenic anemia, eventually develops into Banti's disease.

Histologic study is of little help in solving this problem, for the complete picture as described by Banti is found rather infrequently, while lesions described in splenic anemia are often found in patients who present the clinical picture of Banti's disease. Under the circumstances we feel that it is justifiable to assume that fully developed Banti's disease represents merely the terminal stage of splenic anemia and that the two conditions are identical. This opinion is quite generally held and if it is eventually determined to be supported by the facts it will be wise to drop the term Banti's disease from the nomenclature or to recognize Banti's syndrome as one of the stages of splenic anemia. The present loose practice only causes confusion.

Norris, Symmers and Shapiro have expressed themselves as of the opinion that Banti's disease is merely one expression of syphilis in which the spleen is largely involved. They base their opinion upon the assertion that the histological changes found in the spleen in this condition are quite similar if not identical to those found in syphilis. In a number of instances of Laennec's cirrhosis and of *hepar lobatum*, they found large spleens which presented the histological picture as described by Banti, and, in addition, were able to demonstrate unmistakable anatomical evidences of syphilis. They do not make it quite clear whether they include in their opinion all cases of so-called splenic anemia or limit themselves to those instances which correspond closely to Banti's description.

The arguments against this theory are largely of a negative nature. The Wassermann reaction is of but little help in the solution for it is not uniformly positive in tertiary syphilis, and it is conceivable that a patient might suffer from the two diseases simultaneously. The reaction of the condition to splenectomy is not a good criterion for in any condition in which splenomegaly and cirrhosis of the liver are associ-

ated, whether it be primary hepatic cirrhosis, syphilis or splenic anemia, the removal of the spleen is apt to be followed by improvement in the clinical condition. Furthermore, when splenectomy is performed in syphilis, the patient is always subjected to vigorous antisyphilitic treatment. But patients presenting Banti's syndrome have received prolonged and vigorous antisyphilitic treatment without apparent benefit, and, in a few instances, careful search of spleens from such patients has failed to reveal the presence of spirochetes. It is admittedly difficult to explain away their autopsy findings, but many instances of Banti's syndrome have been described in the literature in which the structural changes in the spleen have not corresponded with those described by Banti, and it may be that these authors have encountered either cases which have presented both Banti's syndrome and syphilis or that their cases have been instances of syphilis in which that infection has produced a condition resembling Banti's syndrome. We believe it possible to accept the view that the hypothetical toxins of cirrhosis of the liver, of syphilis and of splenic anemia have similar effects upon tissue and produce similar reactions. We do not believe that all instances of Banti's syndrome are due to syphilitic infection.

The relation of splenic anemia to cirrhosis of the liver is another puzzling feature of this puzzling condition. Some authors believe that the two conditions are identical, while others assert that in splenic anemia the original lesion is situated in the spleen and that organ is the source of the toxin which later produces the lesions in the liver. Further complication is introduced by the observation that, even in primary cirrhosis of the liver, an enlarged spleen may sometimes be detected before the recognition of any involvement of the liver, the so-called precirrhotic splenomegaly. In these cases one must naturally reserve his opinion concerning the designation of the liver lesion as primary. The other symptoms of splenic anemia, that is to say the secondary anemia, the tendency to hemorrhage and the accumulation of fluid in the abdominal cavity are frequent symptoms of cirrhosis of the liver. In advanced cases of either condition, it is admittedly impossible to determine whether the lesion appeared first in the liver or the spleen.

Microscopic study of the organs involved again gives us comparatively little help, for the differences observed are of degree rather than kind. Splenectomy, as mentioned in a preceding paragraph, may be followed by improvement in both conditions. The important influence of alcoholism in the causation of cirrhosis of the liver does not appear in splenic anemia and in this fact we may ultimately obtain help in the solution of the problem. It has frequently been observed that the typical portal cirrhosis with ascites has become comparatively rare since the advent of prohibition in this country. If future observation shows that instances of splenic anemia do not correspondingly decrease in number, we may perhaps be justified in inferring that the two conditions

are different, at least in their causation. Mayo has summed up the discussion as follows: "At the present we may argue that if the discovery of an enlarged spleen is made first, and of the portal cirrhosis later, the condition is splenic anemia. On the contrary, if there is a history of alcoholism or pepper addiction and the condition of the liver is noticed first and that of the spleen later, we may say that the trouble is primary in the liver and that the splenomegalia is secondary to the liver changes." This begs the question but is probably the best that can be said at the present time. The two conditions may often be distinguished clinically but cannot be shown definitely to be independent.

The situation outlined above makes it very difficult to draw conclusions from many of the cases reported in the literature. Published descriptions are frequently so incomplete that it is impossible to judge what the condition actually is and at times the evidence seems to suggest that the condition is probably not true splenic anemia. For instance in one paper (Fuhs), a case is presented as one of Banti's disease and yet the patient had a positive Wassermann reaction and the description of the spleen is strongly suggestive of tuberculosis. Curiously enough the patient is said to have recovered following splenectomy. In addition, one must realize that it is quite possible that the diagnosis as now applied includes a group of independent conditions and does not represent a single clinical entity.

Definition.—Splenic anemia may be defined as a disease of unknown etiology and chronic course, characterized by an enlargement of the spleen which is often enormous and which shows an interstitial splenitis; a secondary anemia which is often of moderate severity; a marked tendency to hemorrhages from the mucous membranes and into the skin and, in the terminal stages, cirrhosis of the liver and ascites.

Etiology.—It is laid down in the definition that the etiology of splenic anemia is unknown and therefore, as soon as we discover a cause for such a condition, it is automatically excluded from this group. The absence of alcoholism in the history of patients with this disease is quite noteworthy. Gastro-intestinal troubles are described in some cases and in children there is not infrequently found a history of rickets. Splenic anemia occurs more frequently in males than in females and its symptoms are recognized usually during early adult life. However, it is not a rare condition in childhood.

It has been suggested that the splenic enlargement is due to a chronic inflammatory process which results in increased functional activity (hemolysis) and, therefore, anemia (Pearce). Many attempts have been made to discover a bacterial cause for the disease. Various organisms have been isolated from extirpated spleens and injection of some of these bacteria into animals has been followed by the development of a splenomegaly of a type similar to that found in Banti's syndrome (Kristjanson and Yates). But more or less similar results have

been obtained with different organisms and the evidence has nowhere been sufficiently clear-cut to justify definite conclusions. Indeed the fact that different agents may produce similar pictures in the spleen supports the idea that the spleen may react in a similar manner, though perhaps to a different degree, when exposed to a variety of toxic agents. Various types of cocci have been found in these spleens, but the most frequent finding is some member of the diphtheroid group. Unfortunately this group of bacteria is large and its members are found in many of the tissues in a large variety of conditions, and the fact of their pathogenicity has not been satisfactorily settled. Bacteriologists are, therefore, apt to be rather skeptical concerning their significance in those cases in which the only bacterial finding is a member of the diphtheroid group.

Pathology.—We have seen that splenic anemia is rather indefinitely outlined from the clinical side and may expect to find that its pathology is also not sharply defined. It is true that Banti described a definite group of lesions but they are found infrequently and cannot be accepted as being, in their entirety, the characteristic lesions of this disease. The lesions which Banti described are a thickening of the capsule, a fibrosis of the reticulum, a progressive eccentric fibrosis of the malpighian follicles with hyaline degeneration of the arterial walls, an endophlebitis of the splenic vein, an absence of general glandular enlargement, the red bone marrow of secondary anemia and a cirrhosis of the liver of the Laennec type. He has called this complete picture "fibro-adenie." As we have said, these conditions are not often found all together even when the clinical picture corresponds closely with that of Banti's syndrome.

Norris, Symmers and Shapiro claim that the pathological picture can be accurately reproduced by syphilis and they further state that the sclerosis of the follicles is a lesion which is characteristic of recessive status lymphaticus. On the other hand, Nishikawa, after an extensive study of the subject, concludes that Banti's disease is an entity, both clinically and pathologically, and that fibro-adenie is "almost pathognomonic." In his experience, the fibro-adenie of Banti is characterized by marked extension into the pulp of the collagenic and elastic fibers from the thickened capsulotrabecular system; excessive increase and intrapulpos growth of the periarterial elastic, collagenic and lattice fibers with collagenic metaplasia; moderate increase in the intersinuous cords; constriction of the lumina of the sinuses; reduction in the free cellular elements and reduction in number, atrophy and fibrous change of the malpighian follicles by intrafollicular hyperplasia of the periarterial elastic fibers. He claims that in cirrhosis of the liver the spleen shows less thickening of the intersinuous cords, less periarterial elastic hyperplasia, less thickening of the capsulotrabecular system and less regularity in the atrophy of the follicles. Furthermore, he found in Banti's disease no siderosis, no stasis and a much more frequent endo-

phlebitis of the splenic and portal veins. In syphilis, he found that the periarterial elastic overgrowth and fibrosis of the follicles is relatively slight in extent as compared with that found in the spleen in Banti's disease. It will be seen that this author's claims are apparently based upon his ability to distinguish relatively small differences in the degree of pathological change discoverable upon microscopic examination of the spleen. Such a claim makes an insecure foundation upon which to build the assertion that Banti's disease is a distinct entity, both clinically and pathologically. Certainly his descriptions of his findings in cirrhosis of the liver, syphilis and Banti's disease are very similar and give the reader the impression that they represent processes which,



FIG. 36.—SPLENIC ANEMIA.

Young man, subject to epistaxis, about every two weeks, otherwise good health.

Sixteen days before admission vomited considerable bright blood. A few hours later passed several loose black stools. Diarrhea continued for four days. A week before admission, he noticed abdomen had increased in size; no nausea nor vomiting.

Physical examination. Abdomen distended, fluid wave. Spleen extends to level of umbilicus within two inches of midline, not tender.

R. B. C. 2,100,000; hemoglobin, 45 per cent; whites, 4,300 : 2,600. Polymorphonuclears, 77 per cent; lymphocytes, 23 per cent; normoblasts, 2 per cent; a few poikilocytes and microcytes; Wassermann negative.

Operation. Liver smaller than normal with firm round edge and surface slightly nodular. Spleen fixed by numerous vascular adhesions.

while differing in degree and perhaps varying in distribution, are nevertheless essentially similar.

Mitamura takes an even more extreme position. He thinks that Banti's disease, as originally described, is extremely rare and says that it is apparently identical with primary portal thrombosis. In his experience he found no instances of typical annular cirrhosis of the liver but usually an atrophy dependent upon primary liver cell degeneration associated with a sclerosis of the portal vein and its branches. He was able to find no satisfactory evidence of inflammation and no real hyperplasia. He believes that, when marked splenomegaly exists for some

time and is later found to be associated with cirrhosis of the liver, the condition should be considered as essentially a cirrhosis of the liver with a precirrhotic splenomegaly.

Other authors have described various deviations from the usual lesions. Stein and Byfield found spleens in which the sinuses were dilated instead of being compressed. Clark and Rich saw instances in which the malpighian follicles were normal and the former believes the essential lesion to be a primary diffuse hyperplasia. Kettle saw 2 cases with hyperplasia of the follicles and hyaline degeneration. Such atypical pictures are described in the literature in great numbers and it is apparently impossible to differentiate between these cases from the



FIG. 37.—MICROPHOTOGRAPH OF SPLEEN. (From N. Y. H. Path., No. 21,040.)

Splenic anemia. Intense interstitial splenitis with dilatation of the sinuses and thickening of their walls. The fibrosis of the follicle is not well shown.

clinical side. It is obvious that if each author is permitted to limit arbitrarily to a certain definite degree and distribution the lesions of the liver and spleen which are to be considered pathognomonic or even characteristic of Banti's disease, we shall soon have in our literature a series of Banti's diseases in infinite variety. On the other hand, if we accept as true Banti's disease only those cases which present the full clinical and pathological picture as described by Banti, then that condition must be set down as being rare and it will be necessary for us to find a name to attach to the many conditions which conform to its clinical requirements but pathologically deviate from it more or less. In looking at sections from and by studying these cases, one acquires the impression that the pathological lesions found in the spleen

in cirrhosis of the liver, syphilis, Banti's syndrome and splenic anemia in general are all of the same nature. They all appear to be the result of the activity of some toxic agent; and the toxins of syphilis, of cirrhosis of the liver (alcohol) and of splenic anemia seem to produce results that bear a certain degree of resemblance to each other, though they may show enough difference to permit of clinical or even pathological differentiation.

In splenic anemia we find the usual lesions which characterize any secondary anemia and which vary in degree, depending upon the severity of the anemia. There is more or less pallor of the mucous membranes and of the organs, and the bone marrow is red and hyperplastic.



FIG. 38.—MICROPHOTOGRAPH OF SPLEEN. (From N. Y. H. Path., 22,316.)

Splenic anemia. The fibrosis and dilatation of the sinuses are less marked than in the other picture but the beginning degeneration in the center of the follicle is well shown.

The spleen is enlarged, often to a marked extent. The surface is apt to be roughened, because of the presence of areas of perisplenitis, and occasionally presents the typical appearance of the "zuckerguss" spleen. On section, the spleen cuts with some difficulty, and the consistence is found to be increased, being tough and elastic rather than hard. The cut surface is dry and reddish gray and apt to be somewhat roughened by projection of the thickened trabeculae. The malpighian bodies are few in number and smaller than normal. On microscopic examination, the capsule and trabeculae are found to be thickened and from them cords and strands of fibrous tissue, varying in thickness, extend throughout the organ. The lesion is essentially one of interstitial splenitis. There is said to be an increase in the elastic tissue fibers both

in the capsulotrabecular system and extending from it out into the pulp. The venous sinuses are usually compressed but in a few instances have been described as dilated. The intersinuous cords are thickened and the reticulum fibers hyperplastic. The pulp cells are diminished in number and consist only of the normal types of cells. Eosinophils are usually to be found but are not noticeably increased in number. The sinus endothelium is hyperplastic. The malpighian follicles are few in number and are small. They are atrophic, often exhibit a hyaline degeneration and frequently the cell mantle has entirely disappeared from about the central artery. The process is described as an eccentric fibrosis which is said to begin as a hyperplasia of the periarterial elastic



FIG. 39.—MICROPHOTOGRAPH OF SPLEEN. (From N. Y. H. Path., 16,677.)

Splenic anemia. Weigert's stain. The infiltrating fibrous tissue which has taken the blue stain is recognized with difficulty in the photograph. The more dense and narrow streaks are apparent in the upper portion of the picture.

tissue. There is rarely an opportunity for the microscopic study of the splenic lesions early in this disease, for when the patient first visits the physician his spleen is usually extensively involved and the lesion has progressed beyond the early stage.

The splenic and portal veins are often sclerotic, sometimes to an extreme degree, and this feature of the disease sometimes renders the removal of the spleen a dangerous and difficult procedure. The spleen is often attached to neighboring structures by adhesions. The lymph-nodes are not involved in the disease process and are usually quite normal. The lesion in the liver is generally accepted as being the atrophic cirrhosis of Laennec in spite of Mitamura's claims that the

change is more typically an atrophy. His experience has apparently been quite different from that of other writers, including our own. The cirrhosis appears usually comparatively late in the disease and is quite typical both in gross and microscopic appearance. Still later there may be added to the picture an ascites and occasionally a perihepatitis. Varicosities of the veins of the lower portion of the esophagus and of the vasa brevia of the stomach may be demonstrable in those cases in which hemorrhage from the stomach has been a symptom.

Symptoms.—Splenic anemia may be divided clinically into three stages: first, that of splenomegaly and anemia; second, the stage of liver enlargement; third, the terminal stage of ascites.

The stage of splenomegaly and anemia is the longest of the three. It may exist for five or ten or even twenty years. Its exact duration cannot be ascertained for its onset is not recognized. In its beginning, the development of the disease is insidious. The patient first notices that his abdomen is a little larger than it had been or he begins to feel "run down" or his friends tell him that he is getting pale. If he visits a physician, it is discovered that there is already present a well-marked splenomegaly and a mild degree of anemia. Or the enlarged spleen may first be detected in the course of a physical examination made for some other purpose. As the disease progresses, the spleen grows in size. The symptoms of the growing organ differ in different persons. In some, the presence of relatively slight enlargement is accompanied by much discomfort and even acute pain. In others, the spleen may be so large as almost to fill the left half of the abdomen and yet the patient will have experienced only the annoyance of an increasing waist line. Usually, with any well-marked enlargement in the size of the spleen, the patient is conscious of a dragging sensation in the abdomen and a dull, aching pain in the left flank, the lower portion of the left chest or in the left lumbar region. More or less distress after eating may be due to pressure of the large mass on the stomach.

Sooner or later an anemia develops. It may appear suddenly in the form of an acute attack and may recur several times before it becomes permanently established. More often it comes on insidiously and is fairly well marked before it is recognized. The anemia increases slowly in severity, with many remissions or even intermissions, and in the terminal stage of the disease may be severe. It is secondary in type, the color index of the red cells being less than 1.0, usually between 0.5 and 0.7. In extreme instances, the erythrocytes may fall as low as 2,000,000 and the hemoglobin to 25 per cent. The occurrence of large hemorrhages, especially those from the stomach, may result in exacerbations of the anemia; but these are usually quite temporary and the hemoglobin rises quickly to the figure found before the hemorrhage occurred. The anemia thus appears to be due not to the hemorrhages

which so frequently occur in this disease, but to the destruction of blood within the body.

On examination of the blood, we find that the leukocytes are generally low in number. They are often less than 5,000 per c.mm. and never above 10,000 except during the period immediately following a hemorrhage or in the presence of a complicating infection. The differential count shows no definite deviation from the normal formula. The polynuclear cells tend to be reduced both relatively and absolutely. The lymphocytes and the endothelial leukocytes may show a relative increase, especially when the total white cell count is below 5,000. Abnormal white cells are not found. The red cells retain their normal shape and size but show definite central pallor. Nucleated forms are seen but rarely, and polychromatophilia is infrequent. Reticulated or "vital staining cells" are not increased in number. The fragility of the erythrocytes, as measured by their resistance to hemolysis by hypotonic solutions of sodium chlorid, is not increased. The coagulation and bleeding times are within the normal limits. The number of blood-platelets is also normal. If the Wassermann reaction is positive or if malarial parasites are found in the blood, doubt is thrown upon the accuracy of the diagnosis and it will be necessary to subject the patient to thorough treatment for syphilis or malaria while keeping him under close observation, before it is justified to make a diagnosis of splenic anemia.

During the latter part of the first stage, the patient begins to exhibit a remarkable tendency to hemorrhage from the mucous membranes or into the skin. Purpura, epistaxis, hematemesis, melena, hematuria and uterine hemorrhage have been described. The most severe hemorrhages come from the stomach and occasionally prove fatal. They have not infrequently led to a diagnosis of gastric ulcer. In these cases, the blood is believed to come from esophageal varices or from dilated vasa brevia in the stomach. They may recur from time to time over long periods. Osler mentions one of his cases in which they persisted for twelve years.

Jaundice is an infrequent symptom in splenic anemia, although a number of cases have been reported in which there was recognized a certain amount of icterus, usually slight. It is often difficult in these patients to determine whether they are slightly jaundiced. With well-marked anemia, the sclerae are often slightly yellowish and the diagnosis of jaundice is a matter of opinion. The determination of the icterus index should be helpful in deciding this question. The urine usually contains urobilin and when real jaundice exists may also contain bile pigments. In the advanced stages of the disease, the urine may also contain albumin and casts, but ordinarily both are present in but small quantities.

Associated with the above symptoms, we find also those due to the anemia itself. Weakness is an early symptom which later becomes

extreme. Dyspnea appears only when the anemia is marked. With it is associated some enlargement of the heart over which a hemic murmur may often be heard. The heart is rapid and regular and the pulse soft. The color is pale.

With the onset of definite changes in the liver, the second stage of the disease may be said to begin. The liver is at first enlarged and can be palpated. The surface feels somewhat roughened and the consistence of the organ is hard. This stage is comparatively short, lasting from six to eighteen months. During it, the symptoms which have been present become more marked and those which have not appeared become evident.

The third stage is marked by the onset of symptoms of obstruction in the portal system. When fluid begins to collect in the peritoneal cavity, the patient is in the terminal stage of the disease even though it may be as much as two years before death supervenes. The abdominal fluid accumulates more and more rapidly and requires frequent repetition of paracentesis. The patient becomes more and more anemic and emaciated and finally dies from hemorrhage or inanition. As is the case in so many chronic diseases, the patient's resistance to infection is lowered and he is apt to develop pneumonia or some other infection which not infrequently determines the fatal issue.

The following is the history in one of our cases and shows some of the many ways in which these patients show deviations from the "typical" course and history.

Patient H. D., No. 210,572, nineteen years old, single, was admitted to the New York Hospital, February 20, 1917. His family and past history were negative, except for the statement that at the age of twelve, after having been ill for one week with malaria, he had vomited two quarts of blood. His spleen is said to have been enlarged at that time. Three months before his admission he had vomited some blood after having been seasick.

His present illness began one week before admission with cold, cough, chills and fever. The day before admission he noticed some swelling of his abdomen and some slight pain and vomited some blood. During the next twenty-four hours he vomited blood on three occasions and estimated the quantity lost at about three pints. Following his admission he continued to vomit and lost about 1,500 c.c. of blood.

On examination he presented the adenoid type of facies, well-marked facial acne, nasal obstruction, rather large but not acutely inflamed tonsils and a few palpable lymph-nodes in the cervical region. There was some dullness over the apex of his left lung posteriorly. His heart showed a systolic, hemic murmur over his aortic and pulmonic regions. On examination of his abdomen it was found that the left upper quadrant was filled with a firm mass extending down to the umbilicus. There was a notch in the border of this mass and it was recognized as being a large spleen. The edge of the liver was not palpated.

With the continuation of his bleeding in the hospital his anemia increased. On admission his red cells were 4,300,000 and hemoglobin 50 per cent. Ten days later the red cells were 2,600,000, hemoglobin 27 per cent. The white cells varied between 8,000 and 12,000 and the neutrophile polynuclears were about 85 per cent. The red cells showed marked central pallor and a moderate amount of anisocytosis and poikilocytosis. Wassermann reaction both on the patient and on his parents was negative. The hemolysis of his washed erythrocytes began in 0.58 per cent NaCl and was complete in 0.38 per cent. Vital staining cells numbered about 2.2 per cent of the red cells. His coagulation time was eight minutes. His stools contained blood.

On the day after his admission to the hospital he received an intravenous infusion of 600 c.c. of saline. On March 3, he was transfused with 400 c.c. of blood and his spleen removed. The spleen was firm and adherent. The condition of the liver was not noted. After the operation he developed a phlebitis in his left internal saphenous vein but, in spite of that, convalesced fairly rapidly. His white cells rose to 12,000 and his red cells to 3,500,000 among which were a few normoblasts.

He left the hospital in good condition and was under observation at intervals after that. He was readmitted in November, 1919 (No. 226,689) for the removal of his tonsils which were still large. At that time his red cells were 5,000,000, hemoglobin 93 per cent, white cells 11,800 and polynuclears 60 per cent. He felt pretty well except for some gastric distress after meals. He had had no more hemorrhages. He still complained of his acne. His axillary, cervical and inguinal lymph-nodes were all slightly enlarged, discrete and not tender. The fragility of his erythrocytes had diminished somewhat, hemolysis beginning at 0.48 per cent NaCl and being complete at 0.26 per cent. Vital staining cells were less than 2 per cent.

His spleen weighed 610 gm. and measured 5 by 11½ by 18½ cm. The surface was covered by firm adhesions. The capsule was uniformly thickened, grayish white and opaque. At one point on the outer surface there was a much thickened area measuring 3 by 4 cm. Consistence was tough and leathery. The tension of the capsule was less than normal, "probably due to exsanguination." On section the organ presented a uniform appearance throughout. The cut surface was the color of smoked tongue. The stroma was increased, the trabeculae distinct and the pulp diminished. The malpighian follicles varied in size, some being slightly larger than normal and some small and indistinct. There were no focal lesions. The vessels of the spleen appeared to be in good condition though their walls were slightly thickened.

Microscopic examination revealed the features of a high grade of chronic interstitial splenitis. The trabeculae were increased in number and thickness. The follicles were of varying size and in some of them could be seen a central proliferation of endothelial cells. The pulp of the organ presented everywhere considerable spaces among the

meshes of the coarse reticulum in which were some blood-cells and other unidentified nucleated cells.

In this case, the striking feature was the early appearance of the hemorrhages. It seemed that they must have proved fatal but for the operation and they ceased promptly after the removal of the spleen. The result in this case is what is usually reported as a cure though the interval since the operation is yet too short to permit us to be positive about it.

Course and Prognosis.—The course of splenic anemia is chronic, lasting usually from ten to twenty years when not shortened by some intercurrent infection. Its outcome in adults is usually fatal unless a remission or a "cure" is procured by surgical interference. There appears to be a quiescent type of the disease in which the only symptom is the splenomegaly and a very mild anemia that shows little or no tendency to increase. In this type, it is probable that the first stage is so prolonged that the life of the patient is too short to allow the complete development of the disease. In children, the disease is generally said to be less acute than in adults and the prognosis is more favorable. They not infrequently exhibit a distinct tendency to spontaneous recovery and in that respect resemble von Jaksch's anemia. Death may result from hemorrhage, inanition, portal thrombosis or from intercurrent infection.

Diagnosis.—In spite of the difficulty in accurately defining the disease and presenting a sharp clinical picture, the diagnosis of splenic anemia is usually not very difficult. It is made by exclusion. The possibility of the presence of any of the other conditions in which anemia and splenomegaly are associated must be excluded so far as it is possible to do so. It is necessary to obtain a careful and complete history and to make a thorough study of the blood. If other forms of splenomegaly can be shown to be improbable or impossible and the clinical picture is not inconsistent with that usually seen in splenic anemia, then the diagnosis may be made.

Hemolytic icterus may be recognized by finding the increased fragility of the red cells, the frequent history of acute attacks, the constant presence of jaundice and the finding of large amounts of urobilin in the urine. In a certain number of these cases, the history gives evidence of the familial type of the disease.

The splenomegaly of pernicious anemia is usually readily identified upon examination of the blood. The high color index and the presence of the characteristic abnormal erythrocytes often render the diagnosis easy. In some instances during a remission, when the patient is in good general condition, the blood picture is not typical and the diagnosis may be more difficult. In these cases the history is important. As a rule the spleen is not very large in pernicious anemia. The recognition of absence of free hydrochloric acid in the gastric contents is often suggestive of pernicious anemia.

Gaucher's disease may sometimes be differentiated only with difficulty. Ordinarily the skin and conjunctival lesions will point the way to a correct diagnosis, but in their absence the differentiation may be impossible. In Gaucher's disease the spleen is usually larger, the anemia less severe and the hemorrhagic tendency less marked than in splenic anemia. Patients with Gaucher's disease do not become jaundiced, and rarely develop ascites. Splenic anemia exhibits no familial tendency.

In Hodgkin's disease, enlargement of the spleen without general lymphatic enlargement is exceedingly rare if it ever occurs. Chronic malaria may resemble splenic anemia if the spleen is very large. In this country we seldom see malarial spleens that are as large as those found in splenic anemia. The history is important and the parasites may be found in the blood. In kala-azar, the organisms are usually demonstrable in material obtained by splenic puncture. Osler states that primary pylethrombosis is not distinguishable from splenic anemia. Moschcowitz draws attention to the observation that persistence of the umbilical vein may give the same picture as splenic anemia and that possibility should always be borne in mind.

In the earlier portion of this chapter, the resemblance of cirrhosis of the liver, syphilis involving the spleen and splenic anemia was discussed and it may readily be seen that their differential diagnosis may present a problem that is insoluble. The diagnosis of syphilitic splenomegaly may at times be made by obtaining a careful history and making a thorough search for other evidences of syphilitic infection. A Wassermann reaction is often helpful, but its results must not be accepted as final. Cirrhosis of the liver generally appears rather later in life than does splenic anemia, and alcohol is apt to play a prominent part in its etiology. If the involvement of the liver is noticed first, the diagnosis is usually made of cirrhosis of the liver. If the splenic enlargement is recognized first and there is no history of alcohol addiction, it is called splenic anemia. When Banti's syndrome has become established, it is often impossible to say which of the lesions was primary. Hemorrhages occurring in cirrhosis of the liver are rather more apt to be limited to the gastro-intestinal tract. The spleen in splenic anemia is often much larger than that found in those cases which are accepted as being primary cirrhosis of the liver. It must not be forgotten that syphilis may be present in a patient suffering from either of the other two conditions.

Treatment.—The only effective treatment of splenic anemia is splenectomy. When the patient survives the operation, he almost always exhibits an improvement that is so striking that he appears to be cured. Whether we are in fact justified in accepting the usual statement that splenic anemia is cured by the removal of the spleen, especially in its early stages, is perhaps doubtful. A few cases that have been followed for many years have shown a tendency to a return of some of the symp-

toms (Cushing), but this is no argument against the performance of the operation.

The usual medical treatment directed against the anemia is without more than transient effect and the same can be said of transfusion of blood. The Roentgen rays and radium appear to cause no lasting changes in the disease. When syphilis is present, it should naturally be treated vigorously.

The operation of splenectomy is a serious one in these patients because of the frequent presence of adhesions and the sclerosis of the vessels in the pedicle, especially in the more advanced stages of the disease. And yet the operative mortality is gradually decreasing. Giffin reports a mortality of 12.6 per cent in 71 cases of splenectomy for splenic anemia at the Mayo Clinic. Death, when it follows an operation, is usually due to hemorrhage or shock. When the patient is markedly anemic or has lost much blood, a transfusion shortly before, during or after the operation according to the indications, may make a safe outcome possible.

Some years ago we operated upon a case of splenic anemia which illustrates the value of transfusion as an adjunct to splenectomy in profound anemia. A summary of the case follows:

A woman, thirty-nine years of age, was admitted to the New York Hospital on February 4, 1914, complaining of weakness and a mass in the abdomen. She had come to this country three months before admission. On the voyage she was very seasick and vomited frequently, the vomitus on several occasions containing considerable blood. She also noticed that her stools were very dark. Since then she had felt too weak to work. For nearly twenty years she had had a mass in the left side of her abdomen which had been increasing gradually in size but had never caused discomfort. She had never had an acute illness or malaria.

At the time of admission to the hospital, the patient was poorly nourished, looked anemic, had a yellow, ivory colored skin and yellowish sclera. At the apex and base of the heart, there were fairly loud systolic murmurs. A large mass, evidently the spleen, was palpable in the abdomen. Its limits were 1 inch to the right of the midline; 10 inches below the xiphoid in the midline; 8 inches below the costal margin in the mammary line; 5 inches below the costal margin in the anterior axillary line. The mass was firm, somewhat movable, and not tender. The edge of the liver was palpable 2 cm. below the costal margin. The hemoglobin was 28 per cent; red cells, 1,600,000. The Wassermann reaction was negative and the weight of the patient 102 pounds. The patient was transfused on February 15, 1914, about 600 c.c. being given. Hemolysis resulted. On March 7, the patient began to vomit bright red, bloody fluid, six times in twelve hours, in all 42 ounces. The pulse became rapid, weak and small. An intravenous infusion of 24 ounces of normal saline solution was given. She continued to vomit blood at frequent intervals for the next four days. Her movements at this time

contained considerable blood. On March 26, she had a chill, lasting twenty minutes, and one half hour afterwards a temperature of 104° F., respiration 28, and pulse 124. The temperature ranged from 99° to 102° , between the first and second transfusions. At this time, the patient's hemoglobin was 10 per cent, red cells 900,000, and her condition extremely bad. Her weight was 89 pounds. She was transferred to Surgical Service. A donor for transfusion was obtained and extremely careful tests were made between his blood and that of the patient. On March 31, transfusion was performed by the Lindeman method, about 700 c.c. being transfused. The patient improved considerably and about twenty minutes afterwards her spleen was removed. The upper pole of the spleen was adherent to the diaphragm, and in separating these adhesions a large vein was torn which caused considerable hemorrhage. The patient made an uneventful recovery.

The blood count on several occasions and the pathological report of the specimen are given in detail in the case report by Pool, 1914. The patient was markedly benefited. She was seen recently, about eight years after the operation, and is in good condition.

It is generally conceded that the earlier in the disease the operation is performed, the more probably will a favorable result be obtained. Yet operations performed in the advanced stages of splenic anemia have not infrequently been followed by striking improvement or even apparent cure. As is to be expected, the mortality is higher in these patients. Sweetser has been able to collect 42 instances of splenomegaly with ascites in which the spleen was removed, with a mortality of 26.5 per cent. At least 12 of these cases were instances of other conditions than splenic anemia. He reports a case of his own, a man of thirty-seven, with anemia, splenomegaly, ascites and a history of hemorrhages, whose abdomen had been tapped a number of times. He removed the patient's spleen, and, at the time of the operation, noted that the liver was small and hard and the surface hobnailed. Three weeks after the operation, it was necessary to remove six liters of fluid from the peritoneal cavity, but after this the ascites did not recur. Fourteen months after the operation, the patient was feeling well and working hard; and, on examination, it was found that his liver dullness extended down to the costal margin. This the author considers to be evidence of the enlargement and regeneration taking place in that organ.

The usual explanation of the improvement following the removal of the spleen in splenic anemia is that the disease is located chiefly in the spleen; that the spleen elaborates toxins which are distributed through the body and exert their effects chiefly upon the liver, but also upon the bone marrow and other organs. This explanation is hypothetical and is not supported by any direct evidence. Mayo has pointed out that about one fourth of the blood in the portal vein is derived from the spleen and that the removal of this organ can hardly fail to produce profound changes in this circulation. When the liver is affected, the

reduction in the amount of blood brought to it by the portal vein naturally reduces the functional demand made upon that organ and not only permits it, if not too severely damaged, to take care of material brought to it, but probably also to exercise its well-known regenerative powers and perhaps actually to return to a more nearly normal condition. This change in the portal circulation is probably important not only in splenic anemia, but also in the improvement that follows splenectomy in many of the conditions in which anemia and splenomegaly are associated.

Another possibility deserves some consideration. Pearce and his collaborators have shown that the splenectomized animal is able to receive a larger dose of hemolytic serum without showing jaundice than is the normal animal. Their explanation is that, in the presence of the spleen, the material derived from degenerating red cells is furnished to the liver by the spleen in concentrated form and thus induces jaundice when supplied in comparatively slight excess. In the absence of the spleen, its functions are assumed by organs in different parts of the body (lymph-nodes, bone marrow) from which this material reaches the liver in a more dilute form and, therefore, jaundice results less readily. If one assumes that in splenic anemia the changes in the liver and the spleen are produced by a common cause, or even if it appeared more probable that the disease is due to some perversion of a normal function of the spleen, it is possible to argue, by analogy, that after the removal of the spleen, the hypothetical deleterious agents reach the liver in a more dilute and, therefore, a less dangerous form.

The theory that in the removal of the spleen we remove the seat of splenic anemia is supported by the claim that splenectomy is followed by cure, a claim that is probably not justified, and that the earliest recognized lesion of this disease is in the spleen. The paucity of our information concerning the pathogenesis and etiology of this disease prevents us from reaching any satisfactory conclusions on the subject.

Shall all patients in whom a diagnosis of splenic anemia is made be subjected to a splenectomy? Giffin says, "A demonstration that the splenic enlargement is marked and evidence that the enlargement of the spleen was primary are essential in the decision for surgical treatment in splenic anemia." But that amounts merely to saying that one should have the proper grounds for a diagnosis of splenic anemia before removing the spleen. Mayo has pointed out that in any association of splenomegaly and anemia, removal of the spleen is usually followed by improvement. The conditions with which splenic anemia is apt to be confused, syphilis, cirrhosis of the liver, Gaucher's disease, pernicious anemia, have all furnished to the literature instances in which splenectomy has been followed by improvement and it is improbable that any real harm has been caused by the operation. It is urged that the operation be performed as early in the disease as possible. In view of the favorable results that have been obtained by operation in so

many cases and the high mortality of the disease without operation, we feel that every patient with splenic anemia should be offered the chance of splenectomy unless he shows definite clinical improvement while under observation.

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CHAPTER IX

SPLENOMEGALY ASSOCIATED WITH DISEASES OF THE BLOOD (*Continued*): PERNICIOUS ANEMIA AND LEUKEMIA

PERNICIOUS ANEMIA

Idiopathic, primary or progressive pernicious anemia is also known as Addison's or Biermer-Ehrlich anemia. It was first observed by Combe in 1822 and was quite fully described by Addison in 1855. But it was not until the appearance of Biermer's paper in 1871 that much attention was attracted to the condition and it began to be generally recognized. Since that time the literature has grown to voluminous proportions. It would require too much space to present a study of this disease in full detail and we shall limit ourselves to a rather brief discussion of the condition in general, followed by a rather more detailed consideration of its relation to the surgery of the spleen.

The nature of the disease is obscure. Generally believed to be due to excessive hemolysis produced by some unknown toxic agent, there is little satisfactory evidence to support any of the proposed theories to explain the condition. Similar or identical blood pictures are found at times in carcinoma of the stomach, infestation with the *Bothriocephalus latus*, pregnancy, syphilis, chronic lead poisoning, intoxication of intestinal origin and following repeated hemorrhages. In these conditions, the apparent cause of the anemia is frequently a toxin. A hemolytic toxin has been extracted from the intestinal mucosa of persons dead with pernicious anemia. But it has not yet been possible to demonstrate satisfactorily that a hemolytic toxin is actually present in the body in this disease. Extracts of intestinal mucosa are more or less hemolytic in any disease and the work that has been done with the bacterial contents of the intestine is far from convincing.

The infectious nature of the disease has been frequently suggested but is also lacking confirmation. Culture of the spleen has yielded no valuable information. The fact that the severe anemia in itself favors the development of infections in the body is adequate explanation of the frequency with which infections are encountered in this disease.

In those conditions mentioned above, in which the blood picture resembles that found in pernicious anemia, it is found that if the underlying cause can be removed, the anemia will generally disappear. In pernicious anemia, the underlying cause has not been recognized and is, therefore, not amenable to treatment, consequently the disease

is uniformly fatal. Vogel has pointed out that the blood is not a tissue in the true sense of the word and that, therefore, no anemia can be accurately designated as primary. On the other hand, Zadek has observed that in patients during a remission, the bone marrow, at least in the tibia, is normal and he believes that this shows the disease is not one of the marrow.

Under the circumstances, we are inclined to the belief that pernicious anemia is the expression of the action in the body of some toxic substances of unknown origin and nature, which is either in itself hemolytic or stimulates the normal hemolytic tissues of the body to abnormal activity. The changes in the hematopoietic tissues are probably secondary to the anemia.

Definition.—Pernicious anemia, therefore, is a chronic disease of unknown etiology, in which the predominant symptom is a severe anemia with a characteristic blood picture. It occurs rather more often in males than in females and usually between the ages of thirty and sixty. It is less frequent in old age and rare in childhood. Aside from the blood changes, the chief symptoms are achylia, glossitis and nervous symptoms due to lesions in the spinal cord. Its course is marked by remissions during which the patient may appear to have recovered, but it is uniformly fatal.

Pathology.—Tissue changes are found throughout the body such as are found in any severe anemia. There is marked fatty degeneration of the viscera and that of the heart is apt to be extreme. The changes of greatest interest are those which occur in the organs of the hematopoietic system.

The bone marrow is usually of the erythroblastic type. It is red and contains numerous nucleated red cells of all types. In addition, there is often more or less hyperplasia of the myeloid tissue. In general, there is a reversion to the embryonic type of blood formation. In addition to the increase of erythropoietic tissue in the marrow of the long bones, foci of red cell production are found in the liver and the spleen. The lymph-nodes rarely contain such foci.

The spleen is somewhat larger than normal in the majority of cases, but this enlargement is never striking, rarely exceeding 350 gm. The capsule is smooth and not tense. The consistence is firm. The cut surface has a rusty tint and in it the malpighian bodies are normally visible. On microscopic examination, there is found a slight increase in the capsulotrabecular system and of the fibrous tissue throughout the spleen. The normal structure of the organ is fairly well preserved. The venous sinuses are clearly outlined, often somewhat dilated. The pulp is more cellular than normal and contains an increased number of red cells. The lymphoid follicles are apt to be somewhat smaller than usual but preserve their normal structure. Active phagocytosis of the red cells is apparent and there is an increase in the amount of iron-containing pigment present. The striking lesion is the presence of foci of

red cell formation and often of a moderate amount of myeloid metaplasia.

The liver shows foci of erythropoiesis and often active phagocytosis of red cells. The lateral and posterior columns of the spinal cord frequently show areas of degeneration. The mucous membrane of the stomach is atrophic. There are apt to be a number of minute ulcers in the intestine. Numerous minute petechiae are found in the skin, pleura, pericardium, and intestinal tract and there are apt to be small extravasations of blood in the brain.

Symptoms.—The onset of pernicious anemia is insidious. The patient notices a feeling of languor and weakness and his friends dis-



FIG. 40.—MICROPHOTOGRAPH OF SPLEEN REMOVED IN PERNICIOUS ANEMIA. (From N. Y. H. Path., 21,297.)

Note the dilated sinuses and the congestion.

cover that his color is paler than it should be. By the time these symptoms are apparent, the disease is usually well established. The nutrition remains good. Occasionally the nervous symptoms are the first to make their appearance. The color of the skin is usually characteristic. There is a marked pallor combined with a lemon yellow tint apparent both in the skin and conjunctivae. The color in the eyes may even suggest a mild icterus. Glossitis is usually an early symptom. With the development of the condition, there appear all of the symptoms of a severe anemia: weakness, dyspnea, cardiac palpitation and a light edema about the ankles. Osler has called attention to the fact that these patients may have surprisingly little dyspnea even when extremely anemic. Early in the disease there develops an atrophy of the gastric

mucosa which results in the disappearance of free hydrochloric acid from the stomach contents. This symptom is so constant in pernicious anemia that, in the opinion of many authors, its absence is sufficient to make the diagnosis very doubtful. Degenerative changes in the lateral and posterior columns of the spinal cord result in nervous symptoms which may be merely numbness and tingling, sometimes severe neuritic pains or occasionally symptoms resembling those of tabes. The heart is dilated and frequently shows one or more murmurs, although no valvular lesion can be demonstrated at autopsy. The urine is of low specific gravity and may contain a trace of albumin. Urobilin is frequently present. The spinal fluid is normal.

The blood findings are of the greatest importance both in establishing a diagnosis and in determining the progress of the disease. There is a reduction in both the red cells and the hemoglobin, but the former are reduced to a disproportionately large degree. This is in consequence of the fact that the hemoglobin content of the individual red cell, the color index, is abnormally high. It is on this account that one finds in pernicious anemia red cell counts lower than those seen in any other disease. Counts as low as 200,000 per c.mm. have been recorded. The color index is more than 1.0 and sometimes as high as 1.5. The white cells generally remain low and are often markedly reduced below the normal. In the presence of active infection they may be increased.

In the morphological study of the blood, the first thing that attracts attention is the marked distortion in the shape of the erythrocytes. This fact can be observed in the counting chamber, and the poikilocytosis of pernicious anemia was first recognized in this manner. Many unusual and bizarre shapes have been described. Oval, oblong, "racket" and "pessary" forms are frequent. In addition to this variation of the shape of the red cells, there is also seen well-marked anisocytosis. Microcytes, normocytes and megalocytes are numerous. The variation in the size of the red cells may be the only abnormal feature persisting in the blood during a remission of the disease. Accompanying these variations are abnormalities in staining reaction. Some of the cells present colorless centers and appear as narrow rings. Others, on the other hand, present a distinct basophilic tendency and stain a slaty blue with the Romanowsky stains. Many cells show punctate basophilic stippling. The presence of abnormally large red cells that have a distinctly bluish tint is a suggestive finding in a blood that is otherwise normal. Evidence of active blood regeneration is found in the appearance of nucleated red cells in the film. Normoblasts form the majority of these. They are normal in size and contain a nucleus that is usually intensely pyknotic and sometimes apparently dividing. These cells are generally not polychromatophilic but frequently show basophilic stippling. Megaloblasts are not always present but are seen sooner or later in every case of pernicious anemia. They are large cells containing a rather large nucleus which has a loose radial structure. The cytoplasm of

these cells is usually polychromatophilic and sometimes so intensely blue that they may be mistaken for lymphocytes (Butterfield and Stillman). The character of the nucleus and the peculiar slaty tint of the cytoplasm should enable one to recognize this early type of red cell. It is characteristic of pernicious anemia that the nucleated red cells are apt to appear in showers constituting the so-called "erythroblastic crises."

The white cells show comparatively little deviation from the normal. The reduction in the number is usually chiefly at the expense of the polynuclear cells and there is, therefore, a relative lymphocytosis. The eosinophils are but little affected but may disappear during the active progress of the disease. Myelocytes are found not infrequently and Turck's "irritation" forms are occasionally seen.

During a remission, the blood may become wholly normal; but usually it is possible to discover in it certain features that suggest the presence of a pathologic condition. The most important of these is a high color index and the presence of large red cells which may or may not show polychromatophilia. There has been much discussion whether polychromatophilia in pernicious anemia is due to the presence of an increased amount of hemoglobin in the red cell or to the introduction of some new material which darkens the cell. It reacts in the same way as hemoglobin in the various methods of estimating that substance, and since these patients are able to survive with extremely low red cell counts we are confident that the hemoglobin content of the red cell is actually increased. It is quite possible, on the other hand, that the bluish tint of the polychromatophilic red cell is due, not to increased concentration of the hemoglobin within the cell, but to the presence of some basophilic substance probably associated with immaturity.

The "vital staining" red cells are generally increased except during those periods when there is but little blood regeneration and the disease is actively progressing. The fragility of the red cells is normal.

The platelets are reduced in number, and associated with this reduction is a diminution in the coagulability of the blood. In consequence, patients are liable to have hemorrhages.

The blood volume is diminished, but Denny has been able to show that this reduction is due to the diminution in the number of cellular elements and that the plasma volume is normal.

Occasionally one meets with a case which clinically resembles pernicious anemia but presents a leukocytosis due in part to the presence of numerous myelocytes. The number of erythroblasts is also high in these patients. This condition was first described under the name of leukanemia but it is pointed out by Naegeli that the condition is in all probability an atypical form of pernicious anemia. Symmers concedes that histogenically it is like pernicious anemia but believes it is closely allied to myelogenic leukemia.

Course.—One of the most striking features of pernicious anemia is the persistent tendency to the appearance of remissions of the disease. They may occur when the death of the patient seems inevitable or when he is but moderately ill; they may follow the application of some therapeutic measure or appear spontaneously without discoverable cause; they may last but a few weeks or months or for as long as nineteen years (Stockton). Early in the disease, it may be easy to induce a remission by various therapeutic measures, but as time goes on remissions occur at longer intervals or are "induced" with greater difficulty and the patient gradually becomes weaker until death supervenes. The impoverished condition of the blood renders these patients especially susceptible to infection, and they may die at any time from an infectious disease. The occurrence of blood findings similar to or identical with those of pernicious anemia, associated with causes susceptible of removal or improvement, introduces a certain amount of difficulty into the subject of diagnosis. Cases have been described in which the blood picture has been "typical" and no cause has been discovered and yet the patient has recovered. We feel that true pernicious anemia will invariably show remissions and invariably end fatally. Those instances which have been reported as recovered will on examination probably show that the apparent recovery was merely the establishment of a remission; or that the lack of any history of remissions casts doubt upon the accuracy of the diagnosis. We know of no instance of the recovery of a case of undoubted, true pernicious anemia.

Diagnosis.—Pernicious anemia shows three stages which are more or less sharply separated one from the other. During a remission, the patient may seem and feel perfectly well and it may be difficult or impossible to obtain sufficient evidence upon which to make a diagnosis. During the stage of progression of the disease, blood destruction is the dominating factor, blood regeneration is comparatively slight and the patient grows worse. During the stage of regression, blood regeneration dominates the picture and the patient is improving. During the stage of progression, the diagnosis is usually readily made. The history of remissions with achylia and the typical blood picture are together sufficient, as a rule, to establish the diagnosis. We should be reluctant to make a diagnosis of pernicious anemia in the absence of achylia and a high color index, no matter how convincing the other features of the case might be.

The severe anemias of childhood may present difficulties in diagnosis. The color index may be high and the changes in the red cells are often identical with those found in pernicious anemia. But they are frequently associated with a leukocytosis and often yield satisfactorily to treatment. The spleen is usually enlarged to a much greater degree than in pernicious anemia.

The anemias associated with carcinoma or leukemia can ordinarily be distinguished by the features of the blood picture or by a

careful examination of the patient. In those cases in which the carcinoma is not discoverable, the diagnosis may be impossible.

The hemolytic anemia of pregnancy is readily recognized in the course of time since it usually disappears after delivery. Severe cases may end fatally or require the termination of pregnancy. Toxic anemias, in which the nature of the toxin is discoverable, must be excluded from this particular diagnosis. Naegeli has emphasized that in his opinion extraordinary marrow activity is not a feature of true pernicious anemia except as it may occur for brief periods in the erythroblastic crises. Conditions in which such activity is long continued should, therefore, be included under some other diagnosis than pernicious anemia.

Treatment.—We know of no cure or specific treatment for pernicious anemia. Innumerable measures have been applied and, because of the tendency to remission exhibited by the disease, have acquired the credit of benefiting the patients. It is, in fact, extraordinarily difficult to determine whether any measure has real value, for remissions may occur at any time. In the first place, every care should be exercised to free the patient from all recognizable foci of infection and to regulate the intestinal tract so that the absorption of toxic material from that source will be reduced to a minimum. Arsenic has long been used in the treatment of pernicious anemia. It can be given by mouth in the form of Fowler's solution, under the skin in the form of the several cacodylates that are obtainable or into the veins as arsphenamine. Transfusion of fresh or citrated whole blood was first introduced with the idea of supplying thereby some of the deficiency in the cellular elements of the blood. It was soon seen that this operation often resulted in a marked stimulation of the bone marrow and that the improvement in the condition of the patient was far in excess of that attributable to the red cells and hemoglobin he had received. Blood transfusion supplies hemoglobin and platelets, shortens the coagulation time and is often life-saving when the patient is severely ill. But, in addition, it may frequently be followed by the development of a remission in the disease and is apparently the cause of it. The amount of blood to be transfused has been a matter of some discussion, but we are inclined to agree with Hitzrot that small or moderate transfusions, repeated at intervals, have a stimulating action on the blood-forming organs and are less apt to cause unpleasant reactions. It is said that large transfusions may depress the rate of red cell formation but they are occasionally essential in order to save life. The use of a patient with polycythemia as a donor did not result, so far as we could ascertain, in a greater degree of benefit than in any other instance. Transfusions of from 200 to 300 c.c. of blood may be given at weekly intervals until it is apparent that a remission is to be established or until the condition of the patient is so improved that he can get along well without them. Percy advises larger amounts, that is, 500 to 800 c.c. at intervals of 7 to

15 days. Transfusions of quantities up to 2,000 c.c. have been recommended by some authors. It is necessary to determine carefully whether the blood of the donor is compatible with that of the patient, for the latter is often in such a weakened condition that he is unable to survive even slight unfavorable reactions. In this connection, we wish to recall Karsner's observation that if the patient is in very bad condition his agglutinins may be reduced to a point where they will cause no recognizable agglutination in the blood of a proposed donor. Under such circumstances, it is important to test the compatibility of the bloods by both the direct and the indirect methods.

Pernicious anemia is generally accepted to be a hemolytic anemia. The spleen is believed to be normally the most actively hemolytic organ in the body. It, therefore, occurred to several investigators (Eppinger, De Castello, Klemperer) in 1913, that the removal of the spleen might be of benefit in this condition. It was soon tried on a large scale in several countries and is an operation now frequently done. The indications for the operation are still unsettled, but a study of the literature leads one to the opinion that surgeons are coming to the conclusion that every case of pernicious anemia is at some time a favorable subject for splenectomy, and that if the operation is performed at the proper time the life of the patient will probably be definitely prolonged. It has been observed that in any condition in which anemia is associated with enlargement of the spleen, splenectomy is followed by improvement. Several investigators have demonstrated that the life of transfused red cells is longer after the removal of the spleen. And, in addition, the knowledge that the spleen is an important location for the process of disintegration of the red cells suggests that its removal might be of benefit in any process in which hemolysis plays an important part.

The size of the spleen does not vary directly with the severity of the disease. It may, however, be argued that if the spleen is large it is probable that most of the hemolysis going on in the body is taking place in the spleen. On the other hand, if the spleen is small it seems a justifiable assumption that hemolysis is occurring in other locations. On the basis of such argument, it might be said that splenectomy is indicated in pernicious anemia whenever the spleen is enlarged. But the question is not so simple.

Some surgeons claim that splenectomy should not be considered unless there is definite evidence of hemolysis, such as the presence of urobilin in the urine, an increased amount of urobilin in the stools or an increased amount of urobilinogen in the duodenal contents. Hitzrot, on the other hand, feels that the presence of vital staining cells offers a better criterion as to the probability of benefit resulting from splenectomy. It seems to us that the situation is best expressed by the statement that if the diagnosis of pernicious anemia is assured and the study of the patient yields evidence that the hematopoietic system is

capable of sustained activity, then splenectomy is apt to be followed by improvement in the condition of the patient. It is possible that the presence of an increased number of vital staining cells is a better indication of the capacity of the bone marrow than the presence of erythroblasts. It is conceded that these reticulated red cells are young individuals and when their number is large it shows that the marrow is putting out many cells that approximate the mature normal type. Nucleated red cells are immature and, while their presence in the circulating blood is evidence of bone marrow activity, it shows that the process is not entirely normal. When this marrow activity is absent, it may sometimes be induced by the administration of transfusions of whole blood.

The operation of splenectomy in pernicious anemia is not especially difficult, and the operative mortality at the present time is low. Mayo reports 54 splenectomies in this disease with 3 deaths, all of which occurred in the first 19 cases. It is a good procedure to give a transfusion either immediately before or during the operation.

The results of splenectomy are usually good, though some of the reports are conflicting. Moynihan states that, at the Johns Hopkins Hospital, splenectomy for pernicious anemia has been abandoned because they were unable to see any good results after it. On the other hand, Mayo is responsible for the statement that those patients whose spleens have been removed live two and one half times as long as the nonsplenectomized. No one makes the claim that a cure has ever resulted from this or any other method of treatment.

Our experience has led us to the conclusion that the removal of the spleen in cases of pernicious anemia will generally be followed by improvement in the clinical condition of the patient and that this improvement may persist for a long time. Care must be taken to prepare the patient properly by means of transfusions, arsenic, etc., and all foci of infection should previously have been removed. So far as we know, no surgeon has gone so far as to advocate the performance of splenectomy during a remission of the disease. It is possible that this is because of the persistence of the hope that it will not again recur. We know of no case that has been cured. All of our therapeutic measures produce but temporary results; not one of them strikes at the cause. We are able to whip up the marrow by arsenic and transfusions or to lessen the destruction of its product by splenectomy, but we cannot hope to produce any permanent results until we have found the real cause of the trouble. The exposure of the bone marrow to the X-ray seems to us quite contra-indicated.

Summary.—The treatment of pernicious anemia consists primarily in

1. Repeated transfusions.
2. Removal of septic foci.
3. Splenectomy.

The patients usually improve for a time as a result of the transfusions. It is the general opinion that splenectomy should be done when the condition has been rendered sufficiently good by the transfusions to warrant operation. Some authorities, however, prefer to delay splenectomy until remissions of good duration are no longer obtained by means of transfusion (Ottenburg and Libman). The amount of blood recommended for transfusion varies from 200 to 800 c.c., repeated at seven-day to fifteen-day intervals.

Aplastic Anemia.—Occasionally one meets with a patient whose clinical condition suggests a diagnosis of pernicious anemia but in whom, on examination of the blood, we are unable to find any evidence of blood regeneration. Erythroblasts are absent and vital staining cells are few or entirely absent. The leukocyte count is very low (2,000 or 1,500), and there is almost an entire absence of polynuclear cells in the more severe forms of the disease. It is believed that these findings indicate a marked exhaustion of the bone marrow and the condition has been called aplastic anemia. The marrow of the long bones shows atrophy or hypoplasia, though it may be possible to find areas of erythropoiesis in the rib marrow. The course is rapid and the termination invariably fatal. It is generally classified as a type of pernicious anemia, although Frank and others point out that it is more probably a primary atrophy of the marrow and that hemolysis is absent. It is sometimes called aleukia haemorrhagica. It is more apt to occur in the young and has been described as following intensive X-ray treatment. The use of arsenic and transfusions has been recommended but is usually followed by but little improvement. Splenectomy has been performed in a few cases. Gorke was able to collect 4 cases including 1 of his own, all of whom died within a short time after the operation. He also has introduced an interesting test which he believes will aid in the differentiation of aplastic from other forms of anemia. A count of the blood-platelets is made before and after the injection of 1 mm. of epinephrin. In essential thrombopenia, the platelets increase by four or five times. In pernicious anemia there is an increase, but to a less degree, of about 25 per cent. In both of these diseases the bone marrow is still functioning. In aplastic anemia, on the contrary, there is no increase in the number of platelets following the injection.

LEUKEMIA

The departure from the normal blood picture is more striking and extreme in typical cases of leukemia than in any of the other diseases of the blood. The circulating blood contains so many examples of immature leukocytes that it offers ready opportunity for the study of the development of these cells in a manner not afforded by any other disease. For this reason, the study of leukemia has been undertaken by a large number of investigators since its first, almost simultaneous,

description by Bennett and Virchow in 1845. The literature has reached enormous proportions and the investigations have touched every phase of that branch of medicine which has been called hematology. It would be out of place in a work of this description to include an exhaustive treatise on leukemia. We shall, therefore, present only the more important features of the disease and refer the reader who wishes to study this condition more intensively to the hematological literature.

Leukemia is a disease of the hematopoietic apparatus, in consequence of which there is a permanent increase in the number of leukocytes in the circulating blood. It is possible to divide the instances of this disease into two groups depending upon whether the tissue predominantly affected is that which produces the lymphocytes or that which produces the myeloid series of cells. The first group is called lymphatic, lymphoid or lymphoidocytic leukemia or lymphemia; the second, spleno-myelogenous, myelocytic, or myeloid leukemia or myelemla. Either form may be chronic or acute. All types of the disease are invariably fatal so far as we know.

Chronic Myeloid Leukemia.—Chronic myeloid leukemia is a chronic affection of the myeloblastic tissues of the body characterized by extreme hyperplasia and associated with a less degree of hyperplasia of the other leukoblastic tissues. The disease is marked by a chronic course with progressive anemia and weakness and termination in death as a result of exhaustion or intercurrent infection.

The *cause* of the disease is unknown. It occurs indifferently in both sexes, generally in middle life. It is rare in childhood and practically does not occur in infancy. It has never been possible to demonstrate any infectious element in the disease.

The *onset* of leukemia is insidious. The patient may first complain of weakness and lassitude or may be frightened by the comments of his friends upon his color. A certain number are first seen by gastro-enterologists because of disturbances of digestion or pains in the upper abdomen. In other instances, the first symptoms are caused by the enlarging spleen, and the patient comes to a physician complaining of pain in the left flank, a sensation of weight in the abdomen and enlargement of the waistline. Occasionally the patient is first seen by the ophthalmologist, and Osler mentions one instance in which the diagnosis was made on the basis of the retinal examination.

Symptoms.—Whatever the primary symptoms, the clinical picture is soon dominated by three factors: anemia, weakness and splenomegaly. The majority of the symptoms can be traced to one of these three. Pallor, dyspnea, dilatation of the heart, palpitation, restlessness, insomnia and possibly, to some extent, the hemorrhagic tendency may be attributed to the anemia which, as a rule, is not extremely severe. The weakness is not due wholly to the anemia. It may be an outstanding feature before the hemoglobin is appreciably lowered. Emaciation is not ordinarily a prominent symptom. The splenomegaly increases

gradually and eventually reaches an extreme degree. There is often more or less pain in the flank associated with this growth in the size of the spleen, and pressure upon the stomach is apt to induce disturbances of digestion. There is a sensation of fullness and oppression in the abdomen.

Other symptoms may appear. There may be fever from time to time, but it is usually only slight. Infarction of the spleen may be the cause of acute attacks of pain. The bones may be more or less sensitive. Leukemic infiltrations of the skin are found not infrequently, while petechiae and subcutaneous hemorrhages may appear when the tendency to bleeding is established. This tendency may also show itself by hemorrhages from the nose, gums, ears or gastro-intestinal tract. It usually is a comparatively late symptom. Defects in hearing or vision sometimes develop. The changes in the retina are said to be characteristic. The retina has a chocolate brown color and the arteries and veins are poorly differentiated. There are often grayish white flecks and streaks to be seen, and hemorrhages are not rare.

The lymph-nodes are usually not noticeably enlarged and lymphoid structures like the tonsil show no characteristic or striking change. The cardiac symptoms are believed to correspond to the degree of anemia. A chronic bronchitis often occurs. Ascites has been described frequently and it is said that the fluid obtained by abdominal puncture may contain abnormal leukocytes.

The spleen is enlarged early in the disease, and, in the more advanced stages, it becomes enormous, filling the entire left side of the abdomen and reaching to the brim of the pelvis. As felt through the abdominal wall, it is firm, smooth and not tender. The notches can usually be made out, although the organ may be deformed by the contraction of old infarcts and the notches may be simulated by scars. The liver enlarges after the splenomegaly is established, and, with the spleen, appears to fill the entire abdomen.

Priapism is described as a comparatively frequent symptom and is due to the formation of thrombi in the corpora cavernosa.

The urine generally contains albumin and casts in the later stages of the disease. The uric acid output is increased because of the extreme leukocytosis and consequent increased destruction of nucleoproteins. The uric acid content of the blood is also increased. In spite of this fact, as Naegeli points out, the coincidence of leukemia and gout is extremely rare. He was able, in 1912, to find but four instances and could not be sure that in all four the diagnosis of leukemia was properly demonstrated.

The *diagnosis* of leukemia is substantiated by the blood picture. The viscosity of the blood is generally somewhat increased and because of this it is often more difficult to make satisfactory films than is the case with normal blood. There is a moderately severe secondary anemia in well-advanced cases. The hemoglobin is usually between 40 and 60 per

cent and the red cells between 2,000,000 and 3,000,000. The color index remains at, or a little below, 1.0. There is but little anisocytosis and a moderate amount of poikilocytosis. Polychromatophilia and basophilic stippling are usually well marked, and nucleated red cells are constantly found. These are chiefly normoblasts but occasionally typical megablasts are seen.

The blood-plates are generally increased, sometimes to two or three times the normal number. In spite of this, the coagulation time is often increased so that blood drawn into a vessel exhibits an abnormally wide "buffy coat" which has a peculiar grayish color resembling pus.

The characteristic changes in the blood are to be found in the white cells. These are almost always greatly increased. Counts of 200,000 or 300,000 are not unusual and figures of more than 1,000,000 are on record. Occasionally one finds a case in which the figures are temporarily within the normal limits. Most frequently this reduction is the result of treatment or of an intercurrent infection, but it may be seen when there is no apparent cause. This aleukemic stage of myeloid leukemia is usually transient.

The important feature is, however, not the increase in the number of leukocytes, but the appearance in the circulating blood of immature cells of the myeloid series. The normal leukocytes are absolutely and often relatively increased. The eosinophils are apt to be increased to a marked degree early in the disease. The proportion of Ehrlich's metamyelocytes is also notably increased. Myelocytes, neutrophilic and basophilic, but especially eosinophilic, are present and often reach 25 per cent of the total number of leukocytes. Even earlier forms of the cells in this series appear in the circulating blood. Myeloblasts are almost constantly present and, in some instances of the disease, form the predominant feature of the blood picture. One also sees, at times, large undifferentiated mononuclear cells which are believed by many to be the parent cell of all types of leukocytes. In untreated, frank cases of chronic myeloid leukemia, a glance at a single microscopic field is often sufficient to satisfy the observer as to the diagnosis. In other cases, the abnormal cells may be relatively few. After vigorous treatment, the blood picture may return to so near the normal that an examiner unfamiliar with the case might readily fail to make the diagnosis.

During the course of a complicating infectious disease, the blood picture often tends to return to the normal. The total leukocyte count is diminished until it corresponds approximately to that of the infection. The differential count shows an increase in the polynuclear neutrophils, while the abnormal cells diminish in number or may completely disappear. If the patient recovers from the infection, the blood gradually reassumes the leukemic characteristics during the period of convalescence.

At autopsy, one finds often a moderate enlargement of the lymph-nodes which show myelocytic proliferation in the central sinus. The follicles are hyperplastic. The kidneys may also show leukemic infiltration, and similar foci of myelocytic production may be found in various organs and tissues throughout the body.

The spleen is enlarged, often weighing from 2 to 3 Kg. and may weigh as much as 10 Kg. (Naegeli). Perisplenitis is commonly present and the capsule is irregularly thickened in consequence. On section, the cut surface is grayish or dark red, and is frequently marked by large infarcts. The malpighian bodies are small or invisible. On microscopic examination, the spleen appears to have been transformed completely into myelogenic tissue. It infiltrates the follicles. All stages in the development of the myeloid series of cells can be identified. The connective tissue also shows extensive proliferation.

The liver is enlarged. Foci of myelocyte production may be recognized with the naked eye, though sometimes they are so small as to be identified only with the microscope. There is extensive infiltration of myeloid tissue so that in extreme instances actual atrophy of the liver cells may result.

The bone marrow may be a pale grayish red or yellowish as if it were purulent, or, less often, it may be dark red. On microscopic examination, it is found to be extremely cellular and of the myeloblastic type. The myeloblast is often the predominant cell, though sometimes the neutrophil myelocyte is present in greater numbers than any other type of cell.

The course of the disease is progressive to a fatal termination, though there are often occasional brief remissions. It is rare that an actual intermission occurs. The average duration is generally given as from two to three years, though one not infrequently meets with instances of greater chronicity.

Acute Myeloid Leukemia.—It is rare for a case of myeloid leukemia to run an acute course and some of the instances that have been described have been questioned on the ground that the pathologic findings indicated a chronic process in spite of the fact that the course was a rapid one after the appearance of the first evident symptoms. These are explained as being instances in which the disease remained clinically quiescent during its early stages. The diagnosis is rendered difficult by the fact that in the acute cases there is more often an absence of the typical leukocytosis, and the myeloid cells in the circulating blood are frequently the more immature forms. Myeloblasts and primitive undifferentiated forms may predominate and may be mistaken for the large lymphocytes of an acute lymphatic leukemia. Even the splenomegaly may be absent. Nevertheless the condition does occur, and a number of cases have been described. It occurs at all ages, and cases of myeloid leukemia in young children are rather more apt to be acute. The course of the disease is rapid, terminating fatally after an

illness of from a few weeks to two or three months. The histological findings are similar to those met in the chronic form of the disease. The differential diagnosis from the acute form of lymphatic leukemia may be impossible without microscopic examination of the organs.

Chronic Lymphatic Leukemia.—Chronic lymphatic leukemia is an affection of the lymphoblastic tissue throughout the body, characterized by hyperplasia and consequent active production of lymphocytes. It is a comparatively rare disease, being much less frequent than the chronic myeloid type. It is more chronic in its course and less virulent, though it is almost uniformly fatal.

The *cause* of the disease is unknown. It occurs in both sexes and at all ages. The disease appears gradually, the first symptom being the recognition of an enlargement of the superficial lymph-nodes, sometimes in one place, sometimes in another. These swellings are not tender or painful. Other nodes become involved and the enlargement increases until all of the superficial nodes may be greatly increased in size. The nodes remain discrete, as a rule, and are fairly firm. They do not become harder with the progress of the disease. The spleen is enlarged though not to such a degree as in myeloid leukemia. A mild anemia develops. Pruritus occurs and may become intense. The skin may be pigmented. Disturbances in vision and hearing resemble those seen in myeloid leukemia.

The liver is ordinarily moderately enlarged and is firm. Enlargement of the mediastinal and other internal lymph-nodes may give rise to symptoms resulting from pressure upon other structures. The disease may last for many years, the patient becoming progressively, but slowly, weaker until death ensues from asthenia or from intercurrent infection.

Pathology.—The characteristic pathologic change is an extraordinary hyperplasia of all of the lymphoid tissue in the body. This is evident first in the lymph-nodes and later in all organs and tissues in which lymphoid tissue is present. The lymph-nodes and spleen lose their normal structure and become masses of lymphocytes. The bone marrow shows extensive lymphoid hyperplasia, but myeloid tissue can be recognized in it. The tonsils and thymus show lymphoid deposits. Foci of lymphocyte production are found in all organs and tissues, notably in the liver.

The changes in the blood are characteristic. There is a moderate secondary anemia with the presence of nucleated red cells in the severer forms of the disease. The leukocytes are increased to a somewhat less extent than in myeloid leukemia. Counts of 100,000 or 200,000 are the rule and while total counts of 1,000,000 have been reported they are rare. The stained film shows a predominance of small lymphocytes which generally amounts to 90 per cent and may reach 99 per cent. These lymphocytes show certain abnormalities. The protoplasm is often very small so that the cells appear to be naked nuclei. The

nucleus is apt to be less dense than normal. Degenerated forms are fairly frequent. Occasionally giant forms are seen, and a few instances have been described in which large lymphocytes have been a prominent feature in the blood picture. Azure granules are few or absent in the lymphocytes in lymphoid leukemia.

The *diagnosis* is readily made by the examination of the blood, for the characteristic changes are uniformly present except during the remissions which are not infrequent in this disease.

Acute Lymphatic Leukemia.—Acute lymphatic leukemia does not bear the same relation to the chronic form as does the acute to the chronic type of myeloid leukemia. It presents various clinical aspects so frequently associated with fever and necrotic foci that there is a general feeling that the disease must be infectious in its nature. This impression is supported by the not infrequent observation of extreme lymphocytosis in acute infections such as tonsillitis, instead of the more usual leukocytosis. The most careful search has failed to demonstrate any recognized infectious cause in cases of this disease, but numbers of cases have been described in which the condition appears to lie between an infection and a true leukemia (Butterfield and Stillman). In one instance, a guinea pig, inoculated with emulsified gland tissue from one of these patients, developed tuberculosis.

Acute lymphatic leukemia is the most acutely malignant form of leukemia. Its cause is unknown and its recognition is often difficult. The onset of the disease is comparatively abrupt with headache, fever and marked malaise. Tonsillitis may be an early development, and necroses of the mucous membranes of the buccal cavity are frequent. The patient becomes prostrated early in the disease and a diagnosis of typhoid fever may be made. Later the swelling of the lymph-nodes, either superficial or deep, may appear and indicate the true nature of the condition. A hemorrhagic tendency is established early in the disease in a large percentage of the cases. Bleeding from the gums and mucous membranes throughout the gastro-intestinal tract or into the skin or brain may be severe.

Anemia develops rapidly and becomes severe. Deep lymphoid swellings press upon important structures and produce symptoms of dyspnea, venous obstruction, etc. Complicating infections are frequent in the terminal stages. Fluid may appear in the pleural or pericardial cavities. Retinal hemorrhages are frequent and cerebral hemorrhage may terminate the disease. Necrotic areas in the mouth spread and are the source of much discomfort. The breath is foul. The spleen is enlarged to a moderate extent and the liver may also be increased in size. The bones often become sensitive. The urine contains albumin and casts.

The blood findings are of interest but are less constant than in other forms of leukemia. There is usually a severe anemia which not infrequently is of the pernicious type, with a high color index and extreme

changes in the red cells. Nucleated red cells may be found but are not numerous.

The total number of leukocytes is frequently not increased and may be actually diminished. Later in the disease, leukocytosis is apt to appear but rarely reaches very high figures. Counts of from 30,000 to 50,000 are often met. Increase in the mononuclear cells is the rule, but they may be insignificant early in the disease. The characteristic change in the blood is the increase in the large lymphocytes, undifferentiated mononuclear cells which are called lymphoidocytes by some authors and are believed to be immature lymphocytes. But numerous rare and abnormal forms have been described. The cells may closely resemble myeloblasts or, in some instances, may present curiously folded and convoluted nuclei and an undifferentiated cytoplasm unlike that of any other known cell. Giant forms and irritation forms are frequent. We thus have an abnormal stimulation of the tissues which produce mononuclear cells with resultant blood pictures that may frequently resist satisfactory classification.

Leukemic infiltrations are found in practically all of the organs of the body. The spleen is large. The follicles may be swollen and sharply differentiated from the pulp, but more often the border is indistinct and, in the more chronic cases, there is no recognizable line of differentiation between follicles and pulp. The hyperplasia of the lymphoid structures usually is not as extreme as that seen in chronic lymphatic leukemia. The appearance of the lymph-nodes, on the other hand, is much like that in the chronic type. Necrotic areas often prove to be hemorrhagic lymphomata.

The course of acute lymphatic leukemia is ordinarily a steady progression to a fatal termination within from one to several weeks. Occasionally the progress of the disease is interrupted by remissions.

Treatment.—The treatment of the various forms of leukemia varies somewhat but is uniformly unsatisfactory. In no instance is a cure known to have resulted from treatment. Recovery is practically unknown, although it is said to have occurred in one case of the chronic lymphatic type (Naegeli).

There is no treatment for the acute forms of the disease except that which may be directed toward the temporary relief of distressing symptoms. In the chronic lymphatic form, the best relief is believed to result from the exposure to the X-ray. This agent causes a depression in the lymphoid tissue, and its use in this form of the disease may result in the institution of remissions and a definite prolongation of the life of the patient. The administration of arsenic yields but little if any benefit.

In chronic myeloid leukemia, the application of radium or X-ray to the spleen results in a remarkable improvement in the clinical condition and in the blood picture. In one of our patients, seen by the courtesy of Dr. Hayes, a leukocytosis of about 125,000 and a typical blood picture

changed in three months after six X-ray treatments so nearly to normal that it was with difficulty that abnormal cells could be found in the film. The leukocyte count dropped to 12,000 and myelocytes completely disappeared. An occasional myeloblast could be recognized. This patient is still under treatment. Other instances have shown that radium or X-ray treatment produces improvement both in the total count and in the morphological picture. With intermission of the treatment, the blood gradually returns to the typical leukemic condition. With subsequent periods of treatment and rest, the process is repeated until the disease breaks away from all restraint and the patient dies quickly with the blood showing tremendous numbers of all varieties of abnormal cells. It is unknown whether this final outburst of the myeloblastic tissues is one of the results of X-ray treatment, but it is the universal feeling that this treatment must be applied with the greatest caution and must not be pushed to the limit.

The administration of benzol also results in the reduction of the total number of leukocytes and to some improvement in the differential count. This is not very marked and it is usually impossible to continue the treatment for any length of time because of the irritating action of the drug upon the stomach. A combination of the X-ray and benzol treatments has been highly extolled by several authors who feel that they have obtained better results from it than by other forms of treatment. Arsenic is also reputed to have some efficacy in the disease and is regularly given to the limit of the patient's tolerance.

The size of the spleen soon attracted the attention of surgeons and a number of attempts were made to cure or relieve the disease by the removal of the spleen. The mortality was at first extremely high and the operation was condemned. Death occurred from hemorrhage or from shock. Giffin reported that prior to 1918 there were reported 51 splenectomies in leukemia of which 47 died apparently as the result of the operation. This gives a mortality of 93 per cent. Even Strümpell, in 1920, says that splenectomy is dangerous and useless.

But the result of the work at the Mayo Clinic has brought about a radical revision of our views in this matter. They recognized that the principal danger from splenectomy in leukemia was from hemorrhage, especially from the numerous adhesions which hold the large spleen in its place. They, therefore, have practiced a preliminary treatment of the spleen with radium and subsequent splenectomy after the spleen has diminished in size. This method has been notably successful in diminishing the operative mortality. Mayo has recently reported 29 splenectomies in myeloid leukemia with only 1 death. This reduction of the mortality from 93 per cent to less than 4 per cent is a remarkable achievement and its influence is being generally felt. Toenniessen reviews the subject in reporting a case and quotes eight authors all of whom feel favorably inclined toward the use of this operation in the treatment of leukemia.

Of Mayo's cases, 7 are now alive and have been in good condition for more than three years, 4 for more than four years and 1 for more than five years. He says that he "cannot believe these patients are cured," but their lives have certainly been prolonged. Giffin says that after the operation the patients are less apt to develop a severe anemia but are more apt to have a large liver. He thinks the operation is advisable in the very chronic form of myelogenic leukemia with a fibrous spleen and not a very high leukocyte count, but thinks it of questionable value in the majority of cases.

Atypical Leukemias.—The atypical forms of leukemia deserve brief mention here, chiefly to prevent confusion. Cases are unusual and, so far as we know, the application of splenectomy to any of them has not been made.

Chloroma.—Chloroma corresponds quite closely in its clinical course to acute lymphatic leukemia. There are the same masses of enlarged lymph-nodes, and periosteal tumors are said to be one of the characteristic features. On section, the tumors present a green color that has given the disease its name. In at least one instance, Butterfield described as the predominant cell in the blood a mononuclear cell with a convoluted nucleus.

Pseudoleukemia.—Cohnheim described as pseudoleukemia a condition in which enlarged lymph-nodes and spleen had a gross appearance and histologic structure typical of leukemia, but the blood picture was normal in so far as the leukocytes were concerned. Later this term was promiscuously applied to Hodgkin's disease, lymphosarcoma and other obscure conditions in which there was generalized enlargement of the lymph-nodes without leukemic blood picture. The modern tendency is to drop altogether the use of the term. The true pseudoleukemia of Cohnheim is correctly considered as an aleukemic stage of leukemia and the other conditions are better comprehended if the term "leukemia" is omitted from their nomenclature.

Eosinophilic Leukemia.—Stillman, first, and later Giffin and Aubertin and Giroux described cases of apparent myeloid leukemia with marked predominance of eosinophilic cells, both leukocytes and myelocytes. The mature forms predominated. Giffin's case was autopsied and showed a cellular hyperplasia in the spleen and a hyperplastic, eosinophilic bone marrow. He was inclined to think it was not a true eosinophilic leukemia.

Von Jaksch's Disease.—Anemia infantum pseudoleukemia or von Jaksch's anemia has been considered by some to be related to leukemia. This subject has received attention in the section on von Jaksch's anemia. The histologic changes found in this disease argue against a consideration of the two conditions as closely related.

Leukanemia.—Leube used the term "leukanemia" to describe a condition in which the changes in the white cells in the blood indicated the presence of a leukemia, but in which the anemia was much more

severe than is ordinarily seen in that disease. The appearance of the disease is such as to suggest a combination of leukemia and pernicious anemia. This condition is now generally believed to be not a clinical entity but merely a symptom complex which has been observed in a number of diseases. It has been described in pernicious anemia during a blood crisis, in von Jaksch's anemia, in carcinoma of the bone marrow, in the different forms of acute leukemia and even in severe malarial anemia. The term should, therefore, be used merely to indicate a certain blood picture.

Plasma-cell Leukemia.—Naegeli mentions the possibility of a lymphatic leukemia in which many of the cells are plasma-cells. He is of the opinion that it is a variant of lymphatic leukemia.

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CHAPTER X

SPLENOMEGALY AND DISEASES OF THE BLOOD (CONCLUDED): POLYCYTHEMIA VERA, HEMOLYTIC ICTERUS AND GAUCHER'S DISEASE

POLYCYTHEMIA VERA

The term "polycythemia" indicates merely an increase beyond the normal in the number of red cells in the blood. It occurs quite frequently as a secondary manifestation due to a number of physiologic or pathologic causes or following the injection of any one of a very large number of substances or the performance of certain operative measures (Lamson). It also occurs as a primary condition and as such has been called polycythemia vera, Vaquez's disease, Vaquez-Osler disease, erythrocytosis megalosplenica, polycythemia rubra, and a number of other terms. None of these are wholly satisfactory. A term that is accurately descriptive, such as primary true erythrocytosis with splenomegaly, is too long for general use. We have adhered to the use of polycythemia vera, although it does not express the primary nature of the disease and although erythrocytosis is a better word than polycythemia. But the latter is quite generally used and has come to be associated with the disease.

Definition.—Polycythemia vera is a disease characterized by a persistent increase in the number of red cells in the circulating blood and a peculiar cyanosis, usually associated with splenomegaly, increased blood volume, changes in the retinal vessels and weakness. It was originally described by Vaquez in 1892, but was not generally recognized until after the appearance of Osler's paper in 1903 in which he reviewed nine cases. It is not exceedingly rare. It must be differentiated from polycythemia hypertonica (Geisböck) in which the spleen is not enlarged but in which there is regularly a high blood-pressure and cardiac hypertrophy. The latter condition is very rare.

The essential *etiology* of polycythemia vera is not known. It occurs more frequently in males than in females and usually between the ages of thirty-five and fifty-five. The influence of heredity is apparently slight. Theoretically a number of factors might result in a persistent erythrocytosis: increase in activity of the blood-forming organs, decrease in the activity of the blood-destroying organs, increase in the resistance of the red cells to hemolysis, diminution in the oxygen-combining power of the hemoglobin, a constitutional defect in the gaseous

metabolism or, even more obscurely, a disturbance of the mechanism normally regulating the number of red blood-cells. One or more of these factors have been advanced as the cause of the erythrocytosis.

There is ample evidence that the bone marrow is abnormally active in this disease. A number of cases have shown the presence of nucleated red cells in the circulating blood, and, in the few autopsies that have been held, the marrow is described as being hyperplastic. The administration of radium, X-ray or benzol, whose action is to depress the activity of the bone marrow, is followed by a lowering in the number of red cells (at least in some cases) and an improvement in the subjective symptoms. It may then be admitted that there is an increased production of erythrocytes in this disease.

It has not been possible to show that there is any decrease in the destruction of the red cells. The spleen is large and active and there is apt to be a urobilinuria which may be taken to mean an increase in blood destruction. In fact, the large spleen is generally considered to be spodogenous in type.

The question of the resistance of the red cells to hemolysis in this disease is one that has not been satisfactorily answered. Some investigators have found it increased and others claim that it is normal. Unfortunately our methods for determining this characteristic of the erythrocyte are unusually crude. There is no fundamental reason for believing that these cells will react to hypotonic salt solution or cobra venom or to hemolytic immune sera in the same way that they do to those influences whereby they are broken up in the body, in spite of the fact that they seem to do so in hemolytic jaundice. But, even if they do react to these influences in the same way, it seems probable that the resistance of the red cells plays a part of no importance in the disease.

The theory that the increase in the red cells is secondary to a diminution in the ability of the hemoglobin to combine with oxygen was for a time looked upon with much favor. It is known that life in an atmosphere containing a diminished amount of oxygen could be satisfactorily continued only after the number of red cells became definitely increased. Furthermore it is claimed that, following the administration of oxygen to these patients, there was observed a decrease in the red cell count. But it must be realized that when the number of red cells has been reduced to normal by some other means such as phlebotomy or benzol, the patient always feels much better, which would probably not be the case were the erythremia compensatory in nature. More recent studies have definitely shown that the affinity of the hemoglobin for oxygen is the same as that observed in normal blood and, therefore, this factor must be excluded from consideration.

Studies of the gaseous metabolism have as yet failed to reveal abnormalities which shed any light upon the condition.

One is then justified in concluding that the erythremia is due to a hyperactivity of the bone marrow. But the cause of this hyperactivity

is unknown. It is analogous in some respects to leukemia and has been called a tumor process of the blood-forming organs.

An increase in the number of the red cells has been noted in a number of instances to be associated with tuberculosis of the spleen and, in some cases that were considered to be polycythemia vera, autopsy has revealed the presence of this lesion. But such cases seem to be instances of secondary erythremia and do not belong in the section under discussion. In one instance, there appears to have been some suggestion that the polycythemia might be associated with a disturbance of the endocrine system. Engelking reports a family in which three generations were affected, the grandmother, the mother and five children of both sexes. In these cases the eye-grounds showed the characteristic picture and the red cell counts ranged up to 13,600,000. Several of those affected gave evidence of endocrine disturbance such as late menstruation, infantilism, disturbance of gonads and goiter formation. But this is an isolated observation and it is doubtful if we are justified in considering these cases as primary polycythemia. The preponderance of females among them is in itself enough to make them different from other reported cases.

A few autopsies have been performed in this disease. There has been found general congestion of the organs and especially an engorgement of the portal system. The spleen is usually enlarged and shows congestion and a general hyperplasia of all of the tissue elements. In some instances there have been found areas of myeloidosis. The bone marrow shows a hyperplasia that is both erythroblastic and leukoblastic in a majority of the cases, according to most authorities, although Lucas states that this reaction was absent in about one half of the cases and that there is no characteristic lesion of the disease to be found in all autopsies. Late in the disease, there may be thrombosis especially of the abdominal vessels and infarction of the spleen.

Onset.—The disease begins insidiously. The first symptom to be detected may be cyanosis, or the patient may complain of pain and fullness in the head and weakness. In three instances, the abnormal number of red cells was first noticed some months after splenectomy for Banti's disease (Senator). The cyanosis is one of the characteristics of the disease. It has been variously described as ruddy, purplish or magenta. In our case, it was a rich dark red that showed only a slight bluish tinge. It is generally more marked on the face and hands. The enlargement of the spleen appears early but is subject to marked variations. It is smooth and not tender. With the development of the disease, the patient grows progressively weaker and is apt to suffer from hemorrhages, either beneath the skin and mucous membranes, or from the mucous membranes especially of the gastro-intestinal tract.

The changes in the retina are not constant but are said to be characteristic when present. The veins are markedly distended as far as the periphery of the fundus and may show U-shaped indentations along

their course. In places there may be whitish streaks beside the veins, indicating lymph stasis. There is compression of the veins at the arterial crossings. Blurring of the optic disk is found occasionally.

Nervous symptoms occupy a prominent place in the symptomatology. They have been well summarized by Christian. Vertigo, fullness in the head, headache, ringing in the ears, pain and paresthesia in the extremities, loss of consciousness, thickness of speech, staggering gait and blurring of the vision are all noted in his article. Later in the disease, there may be cerebral hemorrhage with its characteristic symptoms. Cerebral thrombosis or hemorrhage, and sometimes softening without vascular change, have been found to explain these symptoms in some cases. The recognition of the erythrocytosis in these patients is of the greatest importance, for they may closely simulate cases of brain tumor and be in danger of operation for that condition.

The examination of the blood reveals the increase in the number of red cells, which may be as high as 15,000,000 per c.mm. The hemoglobin is also increased, but not proportionately, so that the color index is low. Along with these changes, there is increase in the specific gravity, the total blood volume, the viscosity, the iron content and the fat and lecithin content. The coagulation time is shortened. The oxygen content is increased proportionately with the increase in the hemoglobin. The serum, on the other hand, is changed little, if any, except in so far as it may be relatively diminished in volume. The red cells are said to show a diminished nitrogen content (Herrnheiser). Their resistance to hemolysis in the test-tube has been found to be increased, normal and diminished in different cases at different times. The increased cholesterin content of the blood has been taken to indicate that the cells were protected against the action of hemolytic agents, but the subject has not been satisfactorily settled. The complement content of the serum is normal and therefore diminished as measured in the whole blood. Nucleated red cells are seen at times. Naegeli emphasizes their frequency while other authors have not found them.

The leukocytes may be normal in number or definitely increased. They have been reported as high as 54,000. There is an increase in the polynuclear cells rather than in the lymphocytes, and occasionally myelocytes have been found. The platelets are not affected.

The urine frequently shows a trace of albumin and a few casts. This albuminuria is apt to be orthostatic in type. Urobilin is a frequent finding in the urine. The blood-pressure is normal or moderately increased.

CASE REPORT.—No. 234,503. The patient was a Russian sailor, fifty-five years old. His past history was irrelevant. He was well until four years before admission when he began to suffer with cramplike pains in the legs which compelled him to rest after any short walk. Two years later he began to have bleeding gums. Three years before admission he passed through an attack of influenza without serious consequences. A few months before admission he began to be troubled with

anginoid precordial pain, frontal headaches and blurred vision and his weakness, which had progressed very slowly, became more marked.

He is said to have a very large spleen at one time, but shortly before his admission to the hospital he had received treatment with the X-ray and following that the spleen had diminished in size.

On admission he presented a deep slightly bluish red color and no dyspnea. His teeth showed extensive pyorrhea. There was well-marked arteriosclerosis and his heart was moderately enlarged. The eye-grounds were negative. The spleen was only slightly enlarged, the edge being about one finger breadth below the costal margin on inspiration. It was smooth and not tender.

His red cells numbered 7,500,000 and hemoglobin 115 per cent. Leukocytes 10,200, polys 80 per cent, eosinophils 3 per cent. Wassermann reaction, negative. Blood-pressure, systolic 160, diastolic 120 mm. Hg. Urine and stools, negative.

He was used as a donor in a transfusion to a case of pernicious anemia on one occasion. He was placed on benzol for about one week without apparent effect upon his condition.

The *diagnosis* is made on the red cell count and the inability to find any cause for the erythremia. The differentiation from tuberculosis of the spleen may be a matter of extreme difficulty and is important because of the therapeutic indication, since splenectomy is the only treatment for the latter. In a case of tuberculosis of the spleen, it may be possible to find other foci of tuberculosis in the body. There may be some fever and the large spleen may be tender. Morris has reported two cases which showed cyanosis and splenomegaly but no erythrocytosis and says that they suggest an anerythremic erythremia. Other cases of this type have not been described, but, if there is actually such a condition, its differential diagnosis would often be impossible.

The *course* of polycythemia vera is chronic. The clinical condition of the patients is subject to variations between periods of well-being and periods during which the subjective symptoms are particularly severe. After the disease has been present for years, the patients are apt to develop general arteriosclerosis and chronic nephritis and may die from hemorrhage into the brain or meninges. It is not known whether spontaneous recovery may occur.

Treatment.—Since the cause and nature of the disease are unknown, the treatment is necessarily symptomatic. The symptoms seem to be due largely to the plethora present, and measures directed to the relief of that situation often result in temporary improvement. Repeated venesection has been practiced to a considerable extent. X-ray and radium have been used with different effects, depending upon the observer. It has been recommended that the dose of the X-ray be so adjusted that the bone marrow is depressed and the spleen stimulated (Richards and Herrmann). Benzol has been tried, at times with favorable results. Hurwitz and Falconer obtained satisfactory results with

the use of X-ray applied to the spleen together with the administration of benzol, although they report only one case. A low protein diet and the exclusion of tea, coffee, alcohol and tobacco have been recommended. If the general belief is correct that the splenomegaly is spodogenous in character, then one would expect that the extirpation of the spleen would have an unfavorable effect. In fact, the few patients suffering with polycythemia who have been subjected to this operation have died in a comparatively short time. Recently Mayo has reported a case of polycythemia from whom a spleen weighing 900 gm. was removed. The patient made a good recovery from the operation and apparently recovered completely. This is but one instance, but is significant because of the effect it has upon the generally accepted theories as to the cause and nature of the disease. So far as can be told, the diagnosis seemed well founded, but it is necessary to bear in mind the possibility that this was not a true case of polycythemia.

HEMOLYTIC ICTERUS

In 1890, Wilson described cases of congenital jaundice associated with splenomegaly, and, in 1898, Hayem described similar cases that were acquired. Later the congenital form of hemolytic icterus, as the disease was called, became associated with the names of Chauffard and Minkowski, and the acquired type became known as the Hayem-Widal form of the disease. Chronic hemolytic icterus is a chronic disease characterized by splenomegaly, jaundice, the absence of bile pigments in the urine, the presence of coloring matter in the stools and a diminished resistance of the red cells to hemolysis.

The Chauffard-Minkowski form of the disease may be either congenital or familial. In the congenital cases, the jaundice appears very early in life, while in the familial cases it appears later, usually during childhood. In both of these varieties there is a history of other cases in the family. This familial tendency is rather persistent and is not unusual. Meulengracht states that there have been noted nine families in which this disease has been seen in three generations. The Hayem-Widal form may appear at any time during life but usually during early adult life.

The *etiology* of the condition is obscure. Meulengracht states that the familial type is inherited according to the rule of dominants, one half of the children being healthy and the other half jaundiced. The acquired form may be associated with syphilis or may follow pregnancy, but it is not believed that either of these conditions have any etiological relation to the disease. It is generally believed to be based upon some toxic or infectious cause.

The congenital type occurs indifferently in both sexes, but the acquired form is more frequent in women. An attempt has been made to associate this finding with the greater tendency on the part of

women to develop an anemia and the probability, other things being equal, that the anemia in females will be more severe than in males. Pollitzer, Haumeder and Schablin studied ten cases and noted that the majority of them were of a well-built, broad-shouldered, masculine type and were remarkably well nourished. They gave the appearance of having an abundance of water in their tissues, and these authors state that when the anemia reaches a severe grade the patients readily develop an "edematous diathesis."

The *pathogenesis* of the disease has been explained in two ways. One set of investigators believes that it is essentially an increased fragility of the red cells, in other words, that the cause of the disease is to be found in a perversion of the function of the bone marrow which produces cells that are more easily fragmented than normal cells. According to this theory, the splenomegaly is merely the reaction of the spleen to the presence in the blood of an increased number of cells that are ready for destruction. The other school believes that the cause of the disease lies in the spleen. This organ for some reason is excited to over-activity and destroys more cells than under normal conditions. Neither of these theories is adequate to explain all of the findings in the disease. The increase in the fragility of the red cells is a demonstrated fact in so far as our methods are capable of demonstrating it. It is difficult to understand how the spleen could influence the bone marrow to produce such abnormal cells, yet in a number of the cases in which cure has followed splenectomy, the resistance of the red cells to hemolysis has returned to normal. However, in most of the cases the erythrocyte fragility has remained unchanged after the removal of the spleen, although the patient has exhibited a symptomatic cure. This can be explained on the basis of Pearce's observations on the influence of splenectomy upon the experimental production of jaundice. Pearce and his coworkers found that it required a larger dose of hemolytic agents to produce a jaundice in animals after splenectomy than before. He argues that the disintegration of the red cells takes place in the spleen and that the products of this action are sent to the liver by the portal vein in concentrated form. Under the heavy load of this material, the liver is unable to function normally and jaundice results.

In the absence of the spleen, erythrocyte disintegration takes place in various remote areas of the body, probably the bone marrow and possibly the hemolymph-nodes. Under these circumstances, the products of red cell destruction reach the liver by a longer route and in less concentrated form. The liver is better able to take care of the material, and jaundice results only when red cell destruction has reached a higher degree than is required when the spleen is present. The fact that the removal of the spleen reduces by a large amount the quantity of blood coming to the liver also probably enables the liver to work to better advantage.

It has been suggested that the increased fragility of the red cells

is due to the action of some toxin, either produced in the spleen or in some way activated by it. This suggestion has little evidence to support it and in the form in which it has been proposed can probably be disregarded.

There is nothing characteristic about the pathology of the spleen in this disease. There is deep congestion of the pulp and active phagocytosis of the red cells, both by the macrophages and by the polynuclears. The spleen is always enlarged, sometimes enormously so, and contains an increased amount of iron-containing pigment. The amount of pigment is said to be sometimes so great as to give the organ a dark



FIG. 41.—HEMOLYTIC ICTERUS. SECTION OF SPLEEN. (From N. Y. H. No. 16977.)

There is well-marked congestion and a slight increase in fibrous tissue. Pigmentation can be recognized on close inspection.

appearance like that seen in the chronic malarial spleen. There is usually a slight degree of fibrosis and thickening of the capsule, and areas of perisplenitis may be found. The malpighian bodies are diminished both in number and size. The increased number of red cells present are found almost entirely in the pulp and the sinuses are generally empty and compressed (*see* Fig. 41). The pulp cords are more or less atrophic depending upon the amount of congestion. Myeloid metaplasia is absent. The lesion has been called an interstitial congestion of the spleen.

The liver is often moderately enlarged and occasionally shows a biliary cirrhosis (Moynihan). Active phagocytosis is present and pigmentation is increased. The kidneys and bone marrow are also deeply pigmented. The bone marrow is of the erythroblastic type and offers no histological evidence of any abnormality in the mode of erythrocyte production.

The *symptoms* of the congenital and the acquired types of hemolytic icterus are very similar. In both we find acholuric jaundice, that is, icterus with no bile pigment in the urine and with normal stools, splenomegaly and anemia and a diminished resistance of the red cells to hemolysis. But there is usually a marked difference in the intensity of the symptoms in the two types of the disease. In the congenital or familial form, the patients, as Chauffard said, are "more jaundiced than sick." They may lead normal lives and remain completely free from subjective symptoms. It has been noted that, as successive generations are affected, the disease tends to become more mild. These patients may live to advanced age with no serious inconvenience from their disease.

The acquired form, on the contrary, is much more severe. The disease may begin insidiously with the appearance of a mild icterus which is noted by the patient's friends only after it has been present for some time. Or it may begin violently with the sudden onset of pain and fever and the development of a marked jaundice in an attack that simulates that of obstruction of the common bile duct with a gall-stone. The attack subsides but the icterus persists, though it becomes less intense. After a period during which the patient feels comparatively well, another attack appears. These acute attacks were described by Widal as "crises of deglobulization." With the recurrence of attacks, the anemia appears and increases, and in the absence of treatment may become so severe as to prove fatal.

The jaundice of hemolytic icterus is due to an accumulation in the liver of the products of red cell disintegration to such an extent that the liver is unable to take care of them properly and a certain amount of altered pigment is absorbed into the blood stream. The color of the skin and mucous membranes is that of a mild jaundice and deepens only during the crises. It never becomes dark brown as does a long-standing obstructive jaundice. The urine does not contain bilirubin and the stools do contain stercobilin, their normal coloring agent. This jaundice is not accompanied by itching or a decrease in the coagulability of the blood which indicates that the bile acids are not absorbed into the blood.

In about 60 per cent of the cases, there is found a cholelithiasis, and the crises of the disease may be complicated by a real obstructive jaundice. In such circumstances the urine will contain bile and the feces will be clay colored.

The *blood examination* is of the greatest importance in this disease.

There is found an anemia whose severity seems to depend to some extent upon the sex of the patient. Pollitzer, Haumeder and Schablin found an average of 1,500,000 red cells in six women and of 4,500,000 in four men. The red cells show well-marked anisocytosis with a predominance of microcytes rather than macrocytes. These microcytes are often irregular in shape and have been described as fragmented forms of cells. The occasional high color index that is encountered in this disease has been explained by the assertion that the fragmented forms (*splitterförmigen Mikrocyten*) have been overlooked in the counting chamber. Polychromatophilia is well marked, but granular degeneration is not so frequent. There is a marked increase in the number of reticulated red cells that are stained by "vital" stains. These cells may number from 15 to 50 per cent of the total number of red cells. A few normoblasts are often present and megaloblasts have been found but are relatively rare. The hemoglobin is diminished to a greater extent than the red cells so that the color index is usually less than one.

The number of leukocytes approximates the normal but may be increased during and after an attack up to from 15,000 to 18,000. Myelocytes may be present.

The characteristic finding of the disease, as discovered by Chauffard, is a diminution of the resistance of the red cells to hemolysis by hypotonic salt solution, saponin or hemolytic immune sera. Normally, hemolysis of red cells begins at about 0.44 per cent sodium chlorid and is complete at about 0.32 per cent. In hemolytic icterus, hemolysis may begin in salt solution of a strength of 0.75 per cent and be complete in a strength of 0.55 per cent. It has also been noted that not only is the resistance diminished, but that the difference between the point of beginning and that of complete hemolysis is greater in this disease than normally. Similar results are obtained with either washed or unwashed red cells.

The blood serum generally contains urobilin. Bilirubin is present, as a rule, only during a hemolytic crisis. The urine contains urobilin, often in very large quantities. The amount of urobilin (stercobilin) in the stool and in the duodenal contents is increased to many times the normal amount.

Treatment.—Some instances of this disease require no treatment. It has been mentioned that the familial type may cause practically no inconvenience to the patient who may live to an advanced age without discomfort. The acquired form is more severe and requires active interference. The removal of the spleen is the only form of treatment that has been found to be of value, and it almost always is followed by a symptomatic cure. The operation should not be performed during a crisis. If anemia is marked, the operation may be prefaced by a transfusion of blood. If the spleen is extremely large, it can be reduced in size by X-ray or radium treatment before its removal.

The operation is not attended with any unusual risk in this disease.

The mortality rate will depend somewhat upon the conditions under which the operation is performed. In 1917, Elliott was able to collect from the literature 65 instances of splenectomy with a mortality of about 16 per cent. On the other hand, the Mayo Clinic has removed the spleen from 37 patients with this disease and has had only 1 post-operative death (2.7 per cent). Recovery after the operation is usually rapid and the symptomatic cure complete and permanent. The fragility of the red cells returns to normal in some of the cases, but often remains permanently increased. Moynihan refers to the first case of this disease which was operated upon. The patient had her spleen removed in 1887. She recovered completely. She was examined in 1914 and found to be well except that her red cells still showed an increased fragility.

The operation cannot be considered complete unless it includes an inspection of the gall-bladder for calculi and the removal of this viscus if it is indicated and the condition of the patient permits it. Moynihan also advises the removal of the appendix "in all cases in which the condition of the patient does not prohibit the very slight additional manipulation."

GAUCHER'S DISEASE

In 1882, Gaucher described a type of splenomegaly associated with anemia which was characterized by the presence of peculiar large cells in the spleen. He regarded the condition as a primary epithelioma of the spleen. Up to the present time there have been reported about 30 cases of this disease in which the diagnosis has been satisfactorily established. Gaucher's disease is, therefore, a relatively rare condition though it is probable that its apparent infrequency has been exaggerated by the care that has been taken to exclude the possibility of grouping other types of splenomegaly under this heading.

The most careful studies of the condition which have been made since the appearance of Gaucher's original paper are those of Mandlebaum (1912), Brill and Mandlebaum (1913), Mandlebaum and Downey (1916) and Mandlebaum (1919). The material to be found in these papers has been used freely in the preparation of this article. These authors found that a number of cases had been reported as Gaucher's disease, although the diagnosis either had not been confirmed by pathological examination or was based upon histologic findings which they were able to show did not support such a conclusion. Therefore, in the interests of scientific accuracy, they were led to adopt certain criteria which they felt should be followed in making a diagnosis of Gaucher's type of splenomegaly. In doing this they were forced to exclude several cases in which the diagnosis seemed probable but in which it was not possible to perform splenopuncture, splenectomy or an autopsy and thus to obtain confirmatory evidence. Under the circumstances, it is probably safe to assume that the accepted cases represent only a

portion of the total number of instances of this condition that have come under observation.

Gaucher's disease is known also as large-cell splenomegaly, splenic anemia (Gaucher type) or primary splenomegaly (Gaucher type). It is a condition of unknown etiology which usually begins in childhood and shows a tendency to occur in several members of the same generation in the same family though apparently without hereditary influence. It is characterized by progressive enlargement of the spleen followed by a less marked enlargement of the liver. The patients usually present a brownish yellow discoloration of the skin, a wedge-shaped thickening of the conjunctivae, some tendency to hemorrhage, leukopenia and, late in the disease, an anemia of the chlorotic type. The course is mild and very chronic. Death is almost always due to some intercurrent infection. The characteristic pathologic feature of the disease is the presence in the spleen, and later in the liver, lymph-nodes and bone marrow, of certain large cells which will be described later.

The majority of cases begin in childhood, usually before the age of twelve, and occasionally in infancy. The condition may first become apparent in adult life (cases at twenty-five and at thirty-four years have been observed). But it is not possible in these instances (as in our own case) to show that the disease has not been present for some time before its recognition. Females are affected more often than males, and there is an apparent tendency for it to occur in Hebrews more frequently than in other races. Various toxic and infectious factors have been discussed in connection with the cause of Gaucher's disease, but thus far none has been shown to be of importance. Nothing as to the cause of the disease is known.

CASE REPORT.—The patient was a married Hebrew woman of twenty-five years. Her uncle is said to have had some splenic enlargement and there was a familial tendency to ecchymosis and troublesome epistaxis. During her childhood, measles, pertussis and pneumonia; and a node had been removed from the right side of her neck. Since childhood she had been prone to develop large ecchymotic areas from slight trauma and had suffered with prolonged attacks of epistaxis. She thought that her abdomen had always been rather larger than normal.

The history of her present illness could possibly be dated back to about one year before her admission to the hospital. At that time she found that she tired more easily than before, was bothered with a dull aching pain in the back and began to lose weight. During the six months following this onset, she lost thirteen pounds in weight. Five months before her admission, she fell down some steps and struck on her left buttock where there developed in consequence a large hematoma. She stayed in bed only intermittently for about two weeks and then had a miscarriage. This was apparently complete. While in bed at that time, a large mass was discovered in her abdomen and two weeks later, four months before her admission to the hospital, an exploratory

operation was performed elsewhere under the diagnosis of ovarian cyst. The mass was found to be a huge spleen and no attempt was made to remove it. She recovered from the operation but did not regain her health. She still tired easily, had much dragging pain in her back and a feeling of weight in the abdomen and noted that her abdomen was increasing in size. She found that if she remained in bed, much of the pain and discomfort disappeared.

The patient was admitted to the New York Hospital on January 24, 1921. On examination she was found to be a well-nourished young woman, not acutely ill. Her skin showed none of the brownish discoloration which is said to occur in Gaucher's disease and it was not possible to recognize conjunctival thickening which has been described as characteristic. There were a number of small petechial hemorrhages in the conjunctivae and in the skin of the upper eyelids and upper portion of both cheeks. Following the application of a tourniquet for the purpose of drawing blood, ecchymotic rings developed at the site of the tourniquet on each arm.

The spleen was greatly enlarged, extending to the anterior superior iliac spine on the right side and almost to the pelvis below. It was firm and not tender.

Examination of the blood revealed a mild grade of secondary anemia and some prolongation of the coagulation time. Shortly before the operation the following results were obtained:

Wassermann reaction	negative
Coagulation time	10 min. (capillary pipette method)
Bleeding time	6 min.
Red cells	4,200,000 per c.mm.
Hemoglobin	82 per cent
Color index	0.98
Platelets	260,000 per c.mm
White cells	9,800 per. c.mm.
Differential count:	
Polys neut	60 per cent
Lymphocytes	36 per cent
Large monos	3 per cent
Eosinophils	1 per cent
The urine showed a faint trace of albumin but no casts.	

On January 25, splenectomy was performed by Pool. There was a rather firm band of adhesions at the upper pole but the removal was accomplished without incident. The patient made an uninterrupted recovery. This operation was decided upon for two reasons. First, it seemed impossible that the patient would be able to go through a pregnancy with a mass of that size in her abdomen; second, it was thought that the removal of the spleen would relieve her of much of her discom-

fort. The influence of the splenectomy upon the disease was also considered but was thought to be relatively unimportant.

The vessels of the spleen had been carefully ligated so as to prevent the loss of blood from the organ. With its size and weight thus preserved, it measured 8 by 19 by 35 cm. and weighed 3,080 gm. The shape and color were normal. The capsule was tense and when incision was made into it a large amount of fluid blood rapidly escaped from the spleen. The amount of blood thus lost demonstrated in a striking manner the great difference in the blood content of the spleen in the living state and of that organ as seen when sectioned or in microscopic preparations. An attempt was made to preserve the original blood content but it was unsuccessful. The spleen presented two areas, one near the upper pole and one in the middle of the anterior border, where there was a collection of connective tissue resembling scars. It was



FIG. 42.—GAUCHER'S SPLENOMEGALY.
External surface of spleen. Note the scars at lower margin.

thought possible that these might represent healing of lacerations suffered at the time of her fall or healed infarcts.

On section the cut surface was grayish red in color and smooth. The pulp was not readily scraped off with the knife. The surface had a finely granular appearance which on close inspection was seen to be made up of fine grayish points thickly scattered in a background of light red and a small number of minute points which were very dark red. The malpighian bodies were not recognizable. The capsule did not appear to be thickened. The trabeculae were obscured. Microscopic examination showed the typical picture of Gaucher's disease as it will be described later.

Mandlebaum showed that the lesion of Gaucher's disease was not limited to the spleen, although the splenomegaly is the most prominent symptom and often the first feature to attract attention. The liver, lymph-nodes and the bone marrow are also affected, though probably

later in the disease. The essential lesion is the presence in these organs of certain large cells which are peculiar to Gaucher's splenomegaly and have never been found in any other condition.

The Gaucher cells have certain characteristics by which it is possible to recognize them either in microscopic sections or in films made from the surface of the organ. They generally measure from 20 to 40 micra in diameter, though occasional individual cells may be three or four



FIG. 43.—GAUCHER SPLEEN.
Microphotograph of preceding picture.

times that size. Usually round or oval, they may be compressed into a polygonal form in large masses or they may appear to be drawn out into long strands or syncytial masses. The cytoplasm contains a network of fine wavy fibrils which run in the long axis of the cell and which give it a streaked appearance when cut longitudinally and a stippled look when cut transversely. Irregular colorless areas may be

seen where the fibrils have been crowded apart by the accumulation of some substance which has not yet been identified but is said not to be lipoid in nature. The nuclei are small and irregular and eccentrically placed. Cells with two or more nuclei, even as many as twenty-one, are said to be fairly frequent. Mitotic figures have not been described. Some of the cells may contain a certain amount of pigment. Mandlebaum insists that the cells do not contain lipoid material and his claim is borne out by the chemical work which he has done on material obtained from this disease. In a section of Gaucher's spleen, it is possible to find cells filled with fat granules, but these cells are not numerous and such a finding is not unusual in any spleen. Further it is not always possible to say that these fat containing cells are the characteristic Gaucher cells. Mandlebaum's results suggest that the material in the cells may be a complex combination with the phosphatids.

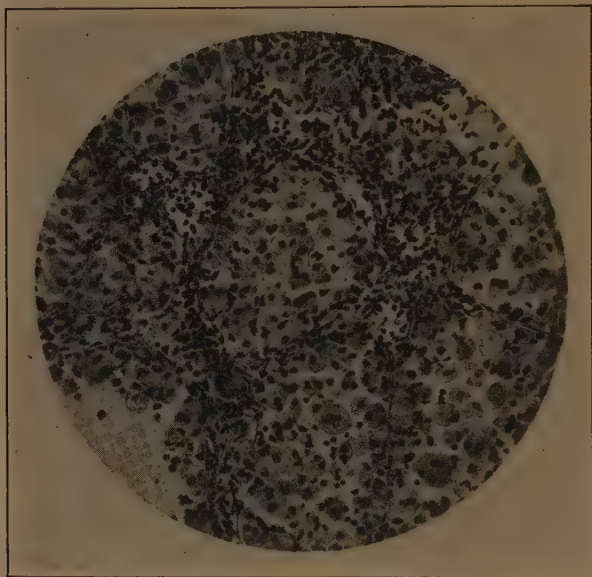


FIG. 44.—GAUCHER'S SPLENOMEGALY.

Section of spleen showing alveoli filled with large cells. The central alveolus is surrounded by a zone of normal pulp cells, and to the right and left small capillaries in transverse section are indistinctly seen. $\times 400$. (Courtesy Dr. F. S. Mandlebaum.)

The question of the histogenesis of these cells is much disputed. Gaucher's idea that they were epitheliomatous in origin did not find acceptance. More recently it has been thought that they may be derived either from the endothelium of the venous sinuses or from the reticulum. In preparations of lymph-nodes, Mandlebaum and Downey observed strands of normal reticulum which finally loosened up and assumed the same structure as the Gaucher cells. They are of the opinion that their studies show "that the characteristic cells of Gaucher's disease are derived from the reticular apparatus of the hematopoietic system, but

the possibility of an additional origin from the endothelium of the venous sinuses in the spleen cannot be denied."

The splenomegaly occurring in Gaucher's disease is one of the largest types we meet. Spleen weights up to 7,400 gm. have been reported. The organ retains its normal form and general appearance. The surface remains smooth until comparatively late in the disease, when there may appear areas of roughening due to the presence of perisplenitis. The capsule is thickened and in our case was distinctly tense. This tension of the capsule quickly disappears if the blood is allowed to escape from the organ. When sectioned, the consistence is found to be firm. The cut surface is brownish pink or brownish red, or, as in our case, grayish red, and is often mottled with white or grayish streaks. Infarcts surrounded by a hemorrhagic zone may be present. The malpighian bodies are few and small or, more often, invisible to the naked eye. The trabeculae are not recognizable.

On microscopic examination, one finds that the normal structure of the spleen has disappeared and in its place the organ is made up of widely dilated venous sinuses in which the characteristic large cells are found. The sinuses may not be completely filled with these cells which have been seen arranged more or less peripherally, leaving a vacant space in the center. The sinuses may or may not be lined with a definite endothelium. The pulp cords are narrow and compressed, but, aside from isolated groups of large cells, their cellular composition remains unchanged. The follicles are few and small but show no other changes beyond a thickening of the walls of the central artery in long-standing cases. There is no increase in the fibrous tissue content of the spleen. Hemorrhagic areas are not uncommon and pigment is invariably present. This pigment is iron containing and increases in amount with the advance of the disease.

The liver is large, light yellowish pink and presents a smooth surface. Older cases may show areas of perihepatitis. On section, the lobules are but faintly indicated and there may be a few grayish streaks seen in the cut surface. The parenchyma is swollen and occasionally exhibits fine hemorrhagic points. Microscopically there is a marked increase in the interlobar connective tissue, and in its meshes are situated the large (Gaucher) cells. The individual liver cells do not appear to be affected. Iron-containing pigment is present in the older cases.

The superficial lymph-nodes are usually not enlarged, but those of the thorax and abdomen always are. Their color is brownish or reddish gray or bright red, or the surface may be pale and the central parts deep red. Later in the disease they may be ocher, deep red or brownish black. They are soft and friable. On microscopic examination, one finds much pigment, fibrosis and diminution or absence of lymph-adenoid tissue. The large cells are abundant, often obscuring the whole structure. The capsule is thickened and the trabeculae are prominent.

The bone marrow is red and generally soft. It may show small white

or yellowish areas. The large cells are found singly or in groups, and reticulum fibers are present between the cells. Pigment is present in small amount only in the advanced cases.

There may be hypertrophy of the lymph-adenoid tissue of the lower ileum and cecum and pigmentation within the muscle fibers of the intestines.

The nature of Gaucher's disease is obscure. Many features of the histologic picture suggest a neoplastic process; and the involvement of the liver, lymph-nodes and bone marrow may be regarded as metastatic. If it is thought to be a neoplasm, it must be postulated that the primary location is in the spleen. On the other hand, the pathologic changes appear to indicate a reaction of one particular type of cell to some peculiar stimulus. The prolonged, benign course of the disease suggests an avirulent type of infection or possibly some disturbance in metabolism. The absence of fever does not invalidate the infection theory and the secondary anemia is rather in its favor. The prominence of the position which the spleen plays in the condition could be explained by its action in filtering the blood and thus concentrating in itself certain infectious organisms. There is no bacteriologic evidence to support the infection theory. The presence of some material (suggested by Mandlebaum to be a protein-phosphatid combination) in the large cells points to an alteration in the body chemistry, but we have no evidence upon which we are able to venture an opinion as to its nature or importance.

The onset of Gaucher's disease is unattended by subjective symptoms. The presence of the enlarged spleen may first be discovered by accident or in the course of a routine physical examination and it is impossible to estimate the duration of the disease prior to this discovery. In some cases, the presence of a huge spleen with its attendant discomfort is the symptom which causes the patient to seek the physician. The growth of the spleen is progressive and is later followed by enlargement of the liver so that these two organs come to fill the peritoneal cavity and give to the abdomen the shape of a barrel.

A peculiar discoloration of the skin is described as one of the early symptoms of the disease though it was not present in our case nor in Foot and Ladd's case. It is a yellowish brown or ocher color which appears in the skin over only those portions of the body which are exposed to light and is frequently deeper across the bridge of the nose and around the eyes. It is not icteric in nature or appearance. Some patients suffer with furuncles at times. Another symptom, which is said to be characteristic and also to appear comparatively early in the disease, is a wedge-shaped thickening of the conjunctivae. This was not present in Foot and Ladd's, Levy's or our own cases. The wedge is placed with its base at the cornea and grows very slowly until the apex reaches the canthus. It affects first the nasal and later the temporal side of the eye and is said to be one of the most constant features of Gaucher's disease. In a case of A. O. Whipple, the discoloration of the skin and the thickening

of the conjunctivae did not appear until 15 months after splenectomy (personal communication).

There is frequently a tendency to hemorrhage from the mucous membranes; and epistaxis, melena and metrorrhagia have been observed. Numerous ecchymoses or petechial hemorrhages may appear in the skin or conjunctivae and the patient may give a history of bleeding freely upon slight provocation. The superficial lymph-nodes are not enlarged with the occasional exception of a few hard nodes in the axillae and groins which rarely exceed 7 mm. in diameter. Jaundice does not occur, and ascites is rare. In the late stages of the disease the patient may suffer at times with pain in the lower ends of the femur and tibia and in the muscles of the thigh and calf. At this stage the nutrition of the patient is interfered with and the emaciation may become extreme. The most prominent symptom of Gaucher's disease is the discomfort which results from the steadily growing spleen. The abdomen enlarges, there is pain in the back, and a dragging pain in the abdomen and lower chest. These pains are relieved by a period of rest in bed and are apt to be aggravated by walking or standing. Constipation may result from pressure upon the intestines.

Leukopenia appears early and persists throughout the course of the disease. White cell counts as low as 200 per c.mm. have been reported and the average is 4,600. There is no disturbance of the normal differential count. In two instances myelocytes have been described, but abnormal leukocytes are not a part of the blood picture. Anemia appears rather late in the disease and is chlorotic in type. The hemoglobin is reduced to a proportionately greater extent than are the erythrocytes, and the color index is consequently low. Normoblasts have occasionally been reported but megaloblasts have not been seen. The average red cell count is given as 3,700,000 and the average hemoglobin as 65 per cent, a color index of 0.87.

The urine shows little that is abnormal. There may be a trace of albumin and a few casts, especially late in the disease. Urobilin is said to be a frequent finding. Bile pigments are never found.

The course of the disease is exceedingly chronic. For years there are few if any symptoms. Then gradually the large and growing spleen produces an increasing discomfort to which there is added later the anemia and emaciation which cause weakness and dyspnea. Death is usually caused by some intercurrent infection or an accident. In the absence of such complications, it is reasonable to expect that the patient would eventually die from exhaustion. The average duration of the disease has been estimated to be nineteen years, and a case lasting for thirty-six years has been reported.

The diagnosis in the early stage is impossible. Gaucher's disease may be suggested when more than one member of a family has combined enlargement of the liver and spleen. The earliest group of symptoms upon which a diagnosis is justified is splenomegaly, enlargement of the

liver and conjunctival thickening with leukopenia and anemia, but without jaundice or ascites. But even in well-established cases, the diagnosis must be made chiefly by exclusion. Occasionally the picture, with the additional symptoms of bronzing, hemorrhagic tendency, etc., is so characteristic that the diagnosis is easy.

It may be difficult to differentiate splenic anemia from Gaucher's disease. Both conditions show chronic splenomegaly, a hemorrhagic tendency, secondary anemia and absence of leukocytosis. But in splenic anemia, the patient shows more pallor, and eventually may become jaundiced. The spleen is generally smaller than in Gaucher's disease, the anemia is more pronounced and appears earlier and there is a greater feeling of distress. The hemorrhages are more general and more severe in splenic anemia, the development of ascites is more frequent and there is no conjunctival lesion.

Hemolytic icterus, leukemia and pernicious anemia should be differentiated from Gaucher's disease by careful and suitable examination of the blood. In Hanot's cirrhosis, there is jaundice. In Hodgkin's disease, one expects general enlargement of the lymph-nodes and the diagnosis can be made by the examination of an excised node. The possibility of there being a form of Hodgkin's disease, in which the spleen alone is enlarged, is doubtful; but such a condition would be differentiated from Gaucher's disease only with difficulty. The conjunctival lesion may be of aid in such a case.

Treatment.—There is no logical treatment of Gaucher's disease. Various preparations of iron and arsenic have been given without any very good reason or satisfactory results. There is no reason to expect that splenectomy should result in a cure, for the disease has been shown to be present in the liver, marrow and lymph-nodes in addition to the spleen. Nevertheless, the removal of the spleen may contribute greatly to the patient's comfort, since it removes a large and annoying mass from the abdomen. In our case there was the additional reason for the operation in the idea that the patient might be able to go through a pregnancy safely after a splenectomy. In 1919, Carr and Moorhead reported that splenectomy had been performed in 9 cases of Gaucher's disease. Of these patients, 2 died as a result of the operation. Of the rest, only 1 was living sixteen months after splenectomy. Apparently the outlook for this method of treatment is not bright. Our patient recovered promptly after the operation and improved greatly. Two years later she was living and apparently well. In the meantime she had gone through a pregnancy normally and had been delivered of a healthy infant.

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CHAPTER XI

OTHER CONDITIONS ACCOMPANIED BY SPLENOMEGALY: TELANGIECTATIC SPLENOMEGALY, RICKETS, GASTRIC HEMORRHAGE OF SPLENIC ORIGIN, PURPURA HEMORRHAGIA

TELANGIECTATIC SPLENOMEGALY

Symmers has recently described a rare systemic disease characterized by extensive proliferation of the endothelium of capillaries, particularly involving organs that belong to the hematopoietic system—the spleen, bone marrow, liver and lymph-nodes. He has seen one case and has found in the literature reports of two other cases which, while they do not correspond exactly to the condition he describes, seem to him to belong to the same group.

His patient was a man of seventy-five who complained only of a dull aching pain under the left costal margin and upon physical examination presented a large spleen and several pea-sized nodules in the skin. These nodules became hemorrhagic after palpation. On the day before death, the skin of the anterior thoracic and abdominal walls suddenly exhibited an extensive network of bluish red or bluish streaks corresponding to congested and dilated capillaries. His hemoglobin was 80 per cent; white cells, 5,400; neutrophils, 69 per cent; lymphocytes, 20 per cent.

At autopsy it was found that the spleen weighed 1,130 gm. and was noticeably soft. It felt like a saturated sponge. On section, the organ was seen to contain innumerable irregular bluish red areas from 1 to 4 mm. in diameter. The pulp tissue was abundant and the malpighian bodies could not be recognized. On microscopic examination, it was found that the structure was readily recognizable as the spleen and that the pulp contained numerous cells both scattered diffusely and arranged in islands frequently tending to arrange themselves about a slitlike or rounded lumen. He interprets them as proliferating young capillary vessels and the cells as endothelial cells. The spleen contained numerous vascular channels of varying sizes all filled with red blood-cells. His impression was that the process was of the nature of an inflammatory reaction rather than of a neoplasm. Similar foci were found in one kidney, in the liver, bone marrow, and in the nodules in the skin.

He described the prominent lesion as a massive enlargement of the spleen due to profuse proliferation of the lining endothelium of its smaller vascular channels with the production of new capillaries and the subsequent formation of telangiectases. He regards the disease as neither

frankly neoplastic nor strictly inflammatory, but presenting features incident to both and perhaps best included in that intermediate group which includes Hodgkin's disease, mycosis fungoides, leukosarcoma and Gaucher's disease.

We have seen no instance of this condition. Whether it will ever demand surgical treatment can only be conjectured. A patient presenting similar symptoms, if in good general condition, might be subjected to a splenectomy with the idea of relieving the symptoms due to the large spleen or of improving the anemia. By analogy with other forms of splenomegaly, the patient would be expected to improve after his operation, but it could not reasonably be expected to bring about a cure of the disease.

RICKETS

Rickets or rachitis is a disturbance of nutrition which manifests itself principally by a defect in the calcification of growing bones. It occurs in children and the etiology is still being actively discussed. A recent article by Hess summarizes the various theories concerning the nature of this disease. According to him, there are three factors which have been shown to be influential in the production of rickets. The lack of sufficient fat-soluble vitamin or phosphorus in the food and the absence of the proper amount of sunlight have all been shown to have something to do with the development of this disease, but it has not been demonstrated that any one of them is, in itself, sufficient to produce it. It seems probable from Hess' summary of the evidence that these factors are closely inter-related and complement one another to some extent. The disease is said not to exist in the tropics, in mountainous countries or in the far north (Strümpell).

An anemia is the rule in this disease. It is usually secondary in type and often not very severe. In a certain number of cases, the anemia is more severe and departs from the simple type of secondary anemia. In these instances the symptom-complex of von Jaksch's anemia develops and the question of a splenectomy arises. For a discussion of this question, the reader is referred to the section on von Jaksch's anemia.

GASTRIC HEMORRHAGE OF SPLENIC ORIGIN

Gastric hemorrhage associated with splenomegaly must be considered under three subdivisions:

1. Obstruction of splenic venous system.
2. Obstruction of portal system.
3. Causative lesion in the spleen.

1. The vascular relations of the spleen, liver and stomach readily explain the incidence of gastric hemorrhage when there is obstruction to the venous flow in the splenic vein. This mechanical factor is illus-

trated most convincingly in thrombosis of the splenic vein where the venous blood from the spleen of necessity passes by way of the left gastro-epiploic and vasa brevia tributaries of the splenic vein to the stomach and thence by anastomoses into the other veins of the stomach. Under such conditions there are produced varicosities in the gastric fundus which readily rupture and cause hemorrhage. Removal of the



FIG. 45.—DIAGRAM OF PORTAL VEIN AND ITS BRANCHES. (By courtesy of Dr. Anders Frick.)

spleen obviously will cure this condition, since the splenic is the only circulatory unit affected. Among the reported cases of thrombosis of the splenic vein with gastric hemorrhage may be cited those of Ringel, Ewald and Frick. The latter has recently contributed an interesting case report of chronic splenomegaly with gastrorrhagia due to thrombosis of the splenic vein. An abstract of the case is appended to this chapter.

2. In cirrhosis of the liver, especially of the portal type, the mechanical element likewise plays an important part both as regards the associated splenomegaly and in causing gastric hemorrhage. This is comparable to the conditions which prevail in chronic adhesive pyelphlebitis and portal thrombosis. In such obstructions of the portal system as a whole, the splenic circulation is only one factor, since the portal obstruction affects all the gastric veins. Therefore, gastrorrhagia may result from obstruction of other vessels than the splenic, and splenectomy, under these conditions, cannot be relied upon for the control of hemorrhage. However, the removal of the spleen will diminish the amount of blood passing to the liver by approximately one fourth and, therefore, might be expected to relieve to some extent the obstruction to other veins of the portal system, thus exercising a beneficial effect.

Portal thrombosis is associated particularly with cirrhosis of the liver, carcinoma of the stomach and pancreas, cholangitis, amyloid disease, splenic anemia and syphilitic cirrhosis of the liver (Webster). The obstruction varies in its extent and produces such symptoms as ascites, splenomegaly, gastric and intestinal hemorrhages and the evidences of a compensatory circulation which are added to those of the primary disease.

There is no support for the theory that gastric hemorrhages in splenic anemia arise from any other than circulatory causes. Whether splenic anemia is assumed to represent a primary disease or is considered as identical with portal cirrhosis of the liver, gastric hemorrhages must be attributed to portal or splenic obstruction.

3. It has been stated that the spleen may be the essential factor in gastrorrhagia in the absence of cirrhosis or with such slight degrees of cirrhosis as could not explain gastric hemorrhage from a mechanical standpoint. How this is brought about, it is impossible to state. Armstrong and Mullaly, in their study of gastro-intestinal hemorrhage with fatal termination, found hypertrophy and fibrosis of the spleen in 2 of the 5 examined cases. Stadelmann, in discussing rare types of hemorrhage in the gastro-intestinal tract, refers to a personal observation of a long-standing case of recurrent and extremely profuse gastric hemorrhage in a syphilitic patient with a well-marked enlargement of the spleen. Death occurred as the result of a severe gastric hemorrhage. At autopsy, no ulcer of the stomach could be found, and the source of the hemorrhage remained obscure. Balfour presents a suggestive case, but even in it there was a moderate degree of cirrhosis and the mechanical factor cannot be excluded. The patient vomited blood repeatedly and became markedly anemic. Several exploratory operations demonstrated absence of duodenal or gastric ulcer, moderate cirrhosis of the liver and a somewhat enlarged spleen (285 gm.). The spleen was removed and Balfour reports that up to seven months later there had been no further hemorrhage, the patient being in good health. Balfour suggests that the bleeding from the mucous membrane may be dependent upon anemia of splenic origin even without splenomegaly or cirrhosis of the liver; or to

some toxic influence from the spleen. Infection may be responsible but, as Balfour points out, while the spleen may act as a primary focus of infection, our present knowledge would indicate that it acts rather as a medium through which infection from a distant focus is transmitted to the liver. The difficulty of diagnosis in such cases is great. Balfour states that "in cases in which gastro-intestinal hemorrhage is the predominating symptom and no ulcer can be demonstrated, the liver should be carefully inspected and a section excised for immediate microscopic examination. Although such gastro-intestinal hemorrhages have been usually attributed to hepatic cirrhosis, recent developments in surgery of the spleen provide a formidable array of facts to throw considerable doubt on the assumption that the liver is the only factor in these cases. Chauffard was one of the first to point out the possibility, in some cases, that cirrhosis is secondary to processes originating, or at any rate most marked, in the spleen."

It is possible that, as a result of a pathological condition of the spleen or coincident with it, there are blood changes which result in hemorrhage from the gastric or intestinal mucosae, and that removal of the spleen corrects this blood condition. But such a hypothesis has little to support it. The whole subject is confused and much more evidence is necessary before conclusions can be formulated.

Analysis of a case which came under our observation throws doubt on the value of splenectomy for gastric hemorrhage in the absence of obstruction to the splenic circulation.

The patient is a young woman who has always lived in New York City; no malaria nor typhoid; had the diseases of childhood. Well until fourteen (1909) when she suddenly vomited a large quantity of blood at night. She was believed to have splenic anemia. Was always tired and weak until eighteen years of age, and had to stop school. Spleen was enlarged all this time. When eighteen, again had a severe hemorrhage, vomiting blood at night, became very weak and was six weeks in bed. Then up and about until twenty-one years of age. She then had repeated hemorrhages, about one a day, and lay in bed very weak for eleven weeks. No other vomiting besides blood. Blood also was passed with stools. Had been anemic more or less since her first hemorrhage which occurred when she was fourteen.

Was admitted to the Post Graduate Hospital on May 26, 1916, with diagnosis of Banti's disease. Her condition was very bad. Blood examination, May 26, 1916, red cells, 1,352,000; leukocytes, 2,400; hemoglobin, 18 per cent. May 31, 1916, 1,416,000 red cells; 2,300 leukocytes; and 18 per cent hemoglobin. At that time it was noted that there was slight poikilocytosis and moderate variation in size of reds. June 3, she received a blood transfusion of 500 c.c. June 6, 1916, red cells numbered 2,248,000; leukocytes, 5,700; and hemoglobin, 28 per cent. The improvement in the blood picture was continuous up to June 30, 1916, when the hemoglobin showed 66 per cent.

She was operated on July 1, 1916, by Dr. J. F. Erdmann. Much difficulty was experienced in delivering the spleen, as it was densely adherent to the dome of the diaphragm, omentum and surrounding structures. The spleen is said to have been very large. The patient had a rather stormy convalescence but was discharged from the hospital on July 28 in good condition. Dr. Erdmann notes that the stomach, intestines and liver were negative at the time of operation.

She gained strength and had no hemorrhages from time of operation until she developed pneumonia five months after operation, when she passed much blood by stool. Had more gastric hemorrhage about ten months after operation. Then had gastric ulcer treatment and was six weeks in bed; was transfused. Improved for a year, then more vomiting of blood and again transfused. Continued to have hemorrhages, at one time seven in two days, but improved without treatment.



FIG. 46.—SPECIMEN OF SPLENIC VEIN WITH THROMBUS. (Courtesy of Dr. Anders Frick.)

No more trouble until January, 1921, at age of twenty-six, when she passed much blood by rectum and fainted. Entered the New York Hospital, June, 1921. X-ray suggested ulcer on the lesser curvature close to the cardiac orifice. Appetite and digestion normal. Bowels regular. Urine normal. Exploratory laparotomy, June, 1921. No ulcer was found after a thorough exploration.

After operation, a number of hemorrhages required several transfusions.

Since leaving hospital, health has been good and has had no further hemorrhage. When last seen in March, 1922, nine months after operation, she was in excellent condition.

In Frick's case (obstruction of splenic vein), the patient was a man, aged sixty-one. When fifty-nine years old he had a small gastric hemorrhage; experienced pain in the epigastrium and became very pale and weak, but recovered rapidly. When sixty years old he had a similar but

somewhat more severe attack. A year later he again experienced sudden epigastric pain and great weakness. After two weeks he became extremely weak, vomited blood profusely and died.

Necropsy revealed an enlarged and not adherent spleen weighing about 500 gm.; an old calcified thrombus in the splenic vein and, immediately to the left of it, another thrombus of recent date. The distal part of the splenic vein, as well as the *venae breves* and the gastric veins, was considerably dilated and there were petechial spots in the gastric mucosa.

The splenomegaly and the gastrorrhagia were due to obstruction in the splenic vein. The normal current in the *venae breves* was reversed; and an increased amount of venous blood was thrown from the spleen through these vessels into the gastric veins, which became engorged and dilated, and finally ruptured.

In regard to diagnosis, Frick states that if a thrombus is located, as in the case reported, in the splenic vein to the left of its junction with the inferior mesenteric vein, it will not interfere with the circulation in any of the portal branches but the splenic vein. If the thrombus had extended farther toward the right, the inferior mesenteric vein would have been occluded, and a formation of hemorrhoids would have resulted. Had the thrombus extended still farther toward the right and into the portal vein, it would have interfered with the circulation in the inferior mesenteric, the duodenopancreatic and the para-umbilical veins. The subsequent passive congestion in the territory of these veins would have caused chronic diarrhea, ascites, enlargement of the superficial abdominal or lower thoracic veins and possibly hemorrhages from the bowels.

PURPURA HEMORRHAGICA

It was not the intention to include a discussion of purpura hæmorrhagica in this work, but while it was in press Brill and Rosenthal presented (New York Academy of Medicine, February 15, 1923) 2 cases of this disease which had been treated by splenectomy with remarkable results. Therefore a brief discussion of the condition is introduced.

Purpura hemorrhagica, morbus maculosus werlhofii or essential thrombocytopenia is characterized by a marked tendency to hemorrhage. Acute cases may undergo spontaneous cure, others become chronic with continuous or intermittent symptoms. The patients bleed, usually from the nose and often from the gums and any or all of the other mucous membranes. The skin is the seat of hemorrhagic spots (petechiae, ecchymoses or suggillations). Spontaneous recovery occurs or the disease terminates in death from anemia and exhaustion.

The onset is usually sudden and the hemorrhage may be slight or profuse. In the continuous form of the disease, the hemorrhages are usually slight and may persist for many years. In the intermittent form, the loss of blood is generally more severe but the intermissions permit

the patient to replace, at least in part, the lost erythrocytes. The diagnosis is made upon examination of the blood. The anemia is usually secondary in type though some instances have been reported in which the color index was high and the picture somewhat resembled that of pernicious anemia. The characteristic feature is a marked reduction in the number of platelets. These bodies vary in number from none to 50,000 or 60,000, but they are always fewer than normal in these cases. In the stained film they are usually seen to be larger than normal as if the megakaryocytes (their source) had not fragmented normally. The coagulation time is normal or slightly prolonged, but the clot does not retract as does that of normal blood. The bleeding time, on the contrary, is prolonged, often to such an extent that it seems unwise to determine its exact length because of the amount of blood that may thus be lost. If a tourniquet is placed about an arm or leg so that the arterial flow is not prevented but the venous return is obstructed, and is allowed to remain for five minutes, petechiae appear in the skin below the tourniquet. This is known as a positive static resistance test.

The spleen is usually enlarged, though sometimes only to a slight degree. On examination it is said to show hyperplasia of the reticulo-endothelial structures, an increase in the number of platelets and hemorrhages. There are frequently hemorrhages in other organs. In one autopsy it was found that the amount of functioning bone marrow was diminished to about one fourth of the normal (Ewing, personal communication).

The treatment has been unsatisfactory. The administration of calcium and the application of adrenalin or thromboplastin is practically without effect. Transfusions may be followed by brief improvement in the hemorrhagic condition, but they often seem to aggravate it and are of no permanent benefit to the patient. Splenectomy was first performed in Europe in 1916 and excellent results have been reported following the procedure.

Brill and Rosenthal's first case was a girl of nineteen who had been bleeding for fourteen years. She was admitted to the hospital with about 18 per cent hemoglobin and 6,000 blood-platelets and the other characteristic features of purpura hemorrhagica. Her spleen was removed and weighed 1,400 grams. She was transfused immediately before and after the operation. There has been no hemorrhage since the operation. The platelets rose to 295,000 but in ten days fell again to 12,000. When shown eleven weeks after her operation, she appeared to be well. Hemoglobin 92 per cent, red cells 6,200,000, platelets 10,000. Bleeding time normal and static resistance test negative but the blood-clot still nonretractile.

The second case was a boy of eleven who had been bleeding for five years. Hemoglobin 30 per cent, platelets 400, other characteristic symptoms present. His spleen when removed weighed 370 grams. His recovery was not so prompt as that of the other patient but when shown

he had 80 per cent hemoglobin and 4,200,000 red cells and was no longer bleeding. His platelets numbered 12,000.

Up to the present, it has been believed that the bleeding which occurs in this disease is dependent upon the characteristic reduction in the number of platelets and that either the spleen destroys an abnormal number of platelets or else in some manner interferes with their production by the megakaryocytes. The observations of Brill and Rosenthal seem to disprove this theory, for in both of their cases the platelets remained low in spite of the fact that the hemorrhages had ceased. They believe that the spleen influences the endothelial cells of the capillaries to exaggerated contraction and that the bleeding is the result of alterations in these vessels.

Whatever the explanation of the effect of the removal of the spleen in hemorrhagic purpura, the results obtained in the few cases on record are so striking that the operation should be performed in all instances that threaten to terminate fatally.

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CHAPTER XII

CYSTS AND NEOPLASMS OF THE SPLEEN

CYSTS OF THE SPLEEN

Nonparasitic Cysts.—Much confusion has been attached to the consideration of nonparasitic cysts of the spleen. This has arisen to a large extent from a tendency to discuss all types collectively. The subject would become much clearer if the various types could be segregated and considered as individual lesions. But the groups are not sufficiently clear-cut from any viewpoint to warrant such a procedure.

The prevailing tendency is to classify spleen cysts according to their pathogenesis, although the modes of origin have not been definitely established. On this basis, Fowler has offered the following classification which has been followed to a large extent by recent writers.

1. Traumatic cysts (hematomata, large unilocular cysts, secondary serous cysts).

2. Infoliation cysts (traumatic or inflammatory inclusions of peritoneum). Small multiple-superficial and deep.

3. Dilatation cysts (ectasia of splenic sinuses).

4. Disintegration cysts (arising from arterial degeneration and occlusion, or other arterial occlusion, as from emboli, and resulting in infarction and necrosis of parenchyma).

5. Neoplastic types (hemangioma and lymphangioma).

6. Degeneration cysts (arising from secondary changes in 5).

It appears unwise to base a clinical classification upon hypotheses. Sufficient facts are available to allow a practical subdivision based upon morphological characteristics. Three distinct types of cysts are noted.

1. Single cysts, usually unilocular, and reaching large size, are the type usually met by the surgeon. These present a nondifferentiated connective tissue wall. They are supposed to be due for the most part to hemorrhage, and consequently have been termed hemorrhagic cysts.

2. Small multiple cysts are often encountered at autopsy and occasionally at operation. They have no clinical significance. They present clear contents and a lining membrane of a single layer of somewhat cuboidal cells.

3. A third rare group consists of innumerable fused cysts involving the whole or a large part of the organ ("polycystic degeneration").

Statistics as to each type cannot be given, since all statistical tables present figures for nonparasitic cysts as a whole. Fowler has reviewed

the more important details in a compilation of 66 cases. In the majority, the disease affected persons in middle life. In only 2 cases were cysts found in infants under one year. Of 65 cases in the series in which the sex was stated, 38 were females. The majority occurred between the ages of twenty and forty, during the child-bearing period. In Monnier's series of 14 cases, 12 were in women. It has been claimed that there may exist a close relationship between pregnancy and cyst formation, but this has not been satisfactorily established. Most of the cases cited in this respect, for instance those of Ghetti, Schallita, Routier, Wells and A. J. Downes, are not convincing. Syphilis has been referred to as of some importance in several cases, notably those of Garcia and Harnett, but analyses of these reports do not indicate any close relationship between the disease and the cyst formation. Garcia's case was probably a cyst of the spleen, but the fact was not proved. Harnett's patient was the subject of advanced arterial disease and had a popliteal aneurysm, cirrhosis of the liver and amyloid disease in the viscera; yet he gave no history of syphilis. It is possible that there may have been a small aneurysm of one of the branches of the splenic artery from the rupture of which the hemorrhage originated, though the absence of any marked disease of the main splenic artery is rather against this assumption.

Attempts to differentiate cysts on the basis of their contents lead to confusion, but it must be stated that besides hemorrhagic cysts containing blood more or less changed, "serous cysts" have been described containing clear fluid of low specific gravity (1003 to 1010), also "lymph cysts" with contents of high specific gravity, and with a tendency to spontaneous coagulation. All three types contain cholesterol (I. P. Lyon, *Osler's Modern Medicine*).

Large Single Cysts (Hemorrhagic Cysts).—The designation "blood-cyst" does not primarily indicate the contents of the cyst, but rather its derivation from a hemorrhage. It is the general opinion of surgeons and pathologists who have written on the subject that most cysts of the spleen which demand surgical intervention are of hemorrhagic origin. Yet the term "hemorrhagic cyst" is unsatisfactory, since it cannot be employed with confidence in all cases. The term "large single cyst," in contradistinction to small multiple cysts, appears better.

These cysts have been encountered for the most part in women, and often in movable spleens. Trauma has been generally accepted as an important etiologic factor. Solieri reported 19 cases in which about 10 had received a direct trauma. The relevancy of these factors appears to be that multiparae with relaxed abdominal walls are prone to develop movable spleens and such spleens are especially subject to traumatism. Monnier, however, believed that the relative frequency in women is due to the periodic hyperemia and changes which the female abdominal organs undergo during menstruation and pregnancy; that during these periods the spleen substance becomes less compact and, therefore, more vulnerable. Bircher suggests as the explanation for the development of

the cyst in his case, embolism, infarction and hemorrhage, following pregnancy. Powers states that we often find recorded an acute exacerbation which brings the patient under medical observation. He regards childbirth as a cause of such exacerbation.

Hemorrhage with resultant development of a cyst apparently may be caused by degenerative changes of the vessels or by embolism. But the resulting cysts in such cases are apparently small and rarely give rise to symptoms requiring surgical intervention.

In a few cases, torsion of the pedicle seems to have been the cause of cyst formation. In Küstner's case, there was undoubted strangulation, which he was convinced was the cause of the large cyst which reduced the parenchyma to a small area. His explanation was that hemorrhage and destruction of splenic tissue resulted in the formation of a cavity. Bircher's case also presented torsion of the pedicle, but this had occurred only a short time before the operation and he felt could be excluded as the cause of cyst formation.



FIG. 47.—CYST OF SPLEEN, SECTIONED.
(Courtesy of Dr. A. V. S. Lambert.)

extent up to about $\frac{1}{2}$ cm. in thickness. The innermost cells may be large and oval or flattened. The wall may show a laminated lining of fibrin as in a large unilocular cyst reported by Musser, which contained old blood pigment. Lambert's report of a hemorrhagic cyst includes a careful description of the wall (Figs 47, 48, and 49). In the growth of the cyst, the spleen may be so compressed that little or no normal tissue is left. Adhesions usually occur between the spleen over the cyst and adjacent structures. Neighboring organs are affected by pressure in proportion to the size of the cyst.

These cysts are most often found at the lower and outer portion of the spleen, which is in support of the influence of trauma as an etiologic factor. The size varies but is often extremely large. Heurtaux reported

a case of a cyst containing more than nine liters; and Maples, a case in which the cyst so completely filled the abdomen that the diagnosis of ovarian cyst was made. The cysts are usually unilocular, yet a cyst may be composed of several communicating pockets.

The contents vary according to the changes in the blood. Usually the fluid is brown and turbid and contains albumin, red blood-cells and cholesterin. The color, however, varies greatly from reddish brown to light yellow and may even be clear.

Large unilocular cysts, which are generally believed to differ from hemorrhagic cysts, have been described in a few instances and have been



FIG. 48.—SHOWS THE SEPTA PROJECTING INTO CYST CAVITY. (Courtesy of Dr. A. V. S. Lambert, *Annals of Surgery*.)

Note splenic pulp persisting in the septum.

termed "serous cysts." The peculiar feature is that the cyst wall is said to present a differentiated cuboid cell lining; the contents, according to Musser, are clear (serous) yellow, with low specific gravity; albumin may or may not be present while cholesterin crystals are invariably found. These cysts give rise to much the same confusion and discussion as the group about to be described. If it is accepted that the lining cells are derived from already differentiated cells (endothelial), these cysts constitute a special type. If, on the other hand, the lining cells are interpreted as being derived from connective tissue stroma cells, the group does not demand individual consideration. We have not encountered an example of this type, but, judging from case reports and the study of the

small cysts about to be described, we are inclined to include these large "serous" cysts with the hemorrhagic cysts, assuming that they have no structural feature which differentiates them from hemorrhagic cysts, or warrants distinguishing two groups of large single cysts.

Small Multiple Cysts.—In contrast to hemorrhagic cysts, these are usually of very small size and are not the type which demands surgical intervention; nor do they present features of clinical significance. It is to this class that attention has been directed in formulating many of the theories as to the pathogenesis of spleen cysts, such as have been advanced by Beneke, Renggli, Ramdohr and Schmidt, Pepere and others.

These minute, usually multiple, cysts of the spleen are found especially along the anterior border on the surface or beneath it. They are rarely

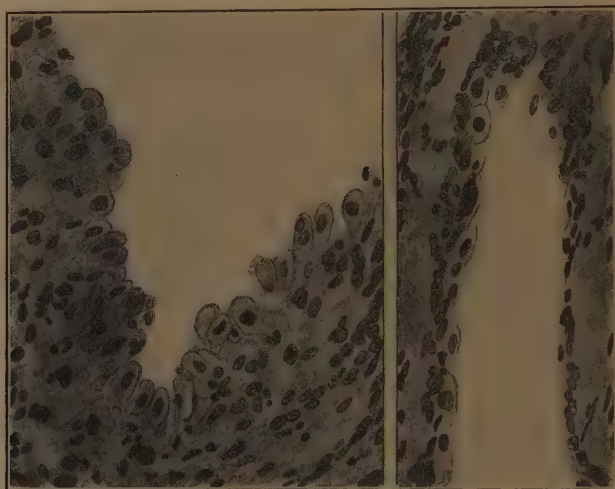


FIG. 49.—SHOWS THE CHARACTER OF THE CELLS LINING THE CYST. (Courtesy of Dr. A. V. S. Lambert, *Annals of Surgery*.)

Note the great variety in form and irregular arrangement.

more than a few millimeters in diameter, but occasionally measure several centimeters. The contents are clear. If the spleen is regularly examined at autopsy, this type of cyst will be noted frequently. The rare specimens of the lesion found in large collections of pathological material and the infrequent records in autopsy reports imply that the condition is not in general recognized or is ignored.

The striking feature of these cysts is the structure of the wall. This usually presents a single row of cells which in general appear cuboid, less often flattened. This feature has excited much discussion as to the histogenesis of these cells. They have been interpreted as of peritoneal origin as the result of embryonal rests or infoldings following capsular rupture or perisplenitis. They have also been attributed to the endothelium of the lymphatic spaces or blood-vessels. These theories will be presented more in detail in a later paragraph. We have examined a number of these cysts in an attempt to ascertain their origin. It has been impos-

sible, however, to determine the nature of the lining cells; and no valid evidence can be found, nor does such seem to have been presented to warrant the adoption of any of the theories as to their histogenesis. On the other hand, the theories cannot be successfully combated. We are, therefore, forced to the conclusion that the histogenesis of these cysts is still uncertain.

Study of the material from our own cases and several cysts from McCallum, Symmers and the Surgeon General's Museum show that the structure of the cyst walls in most of the cases is similar. The wall consists of dense hyaline connective tissue, lined by a single layer of flattened or cuboid cells. These cells somewhat resemble endothelial cells. They are large with round or oval nuclei and clear cytoplasm. A few cells may be seen within the cavity suggesting exfoliated lining cells. The cysts

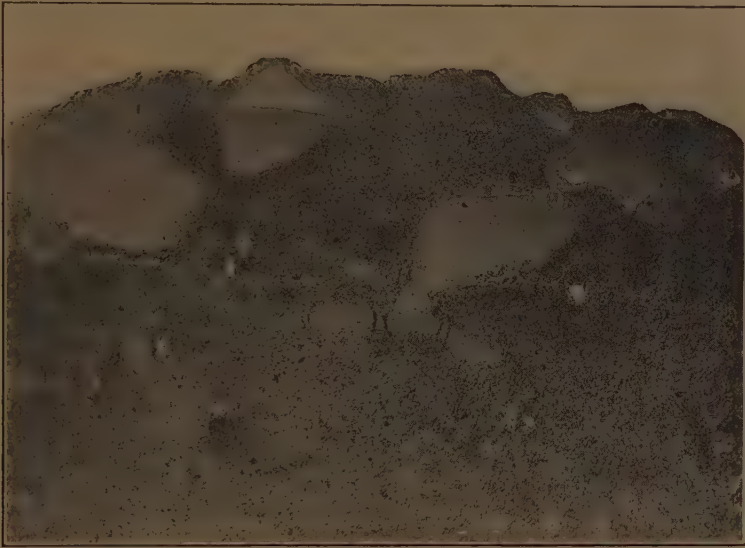


FIG. 50.—LOW POWER OF CYSTS FROM SPLEEN REMOVED AT AUTOPSY.

contain a pink staining homogeneous material resembling coagulated lymph.

A typical case follows. Autopsy 5,571, New York Hospital, Dr. Muller. The spleen weighs 250 gm. Its consistency is normal. Along the anterior margin are several small clusters of clear cysts. These cysts project above the surface, are directly beneath the capsule and average from 1 to 2 mm. in diameter. In the largest group a few cysts are slightly red. They are firm and not compressible. Microscopic: In the section are seen a number of small discrete cavities having a hyaline connective tissue wall and a lining consisting of a single layer of cuboid cells, or cells that are slightly flattened. The contents consist of a pink staining homogeneous material resembling lymph. In this are a few large single cells of which a few contain granules of brown pigment. These cells are probably desquamated lining cells.

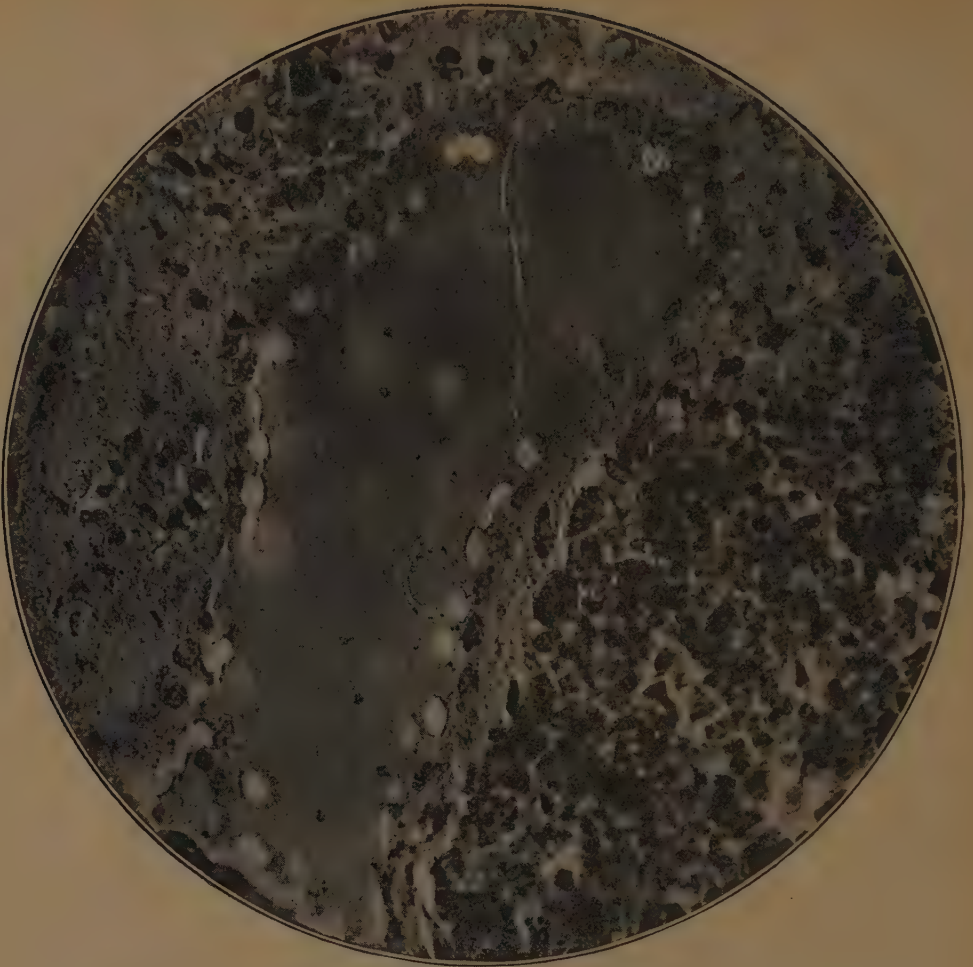


FIG. 51.—HIGH POWER OF PRECEDING PICTURE TO SHOW TYPE OF LINING CELLS.

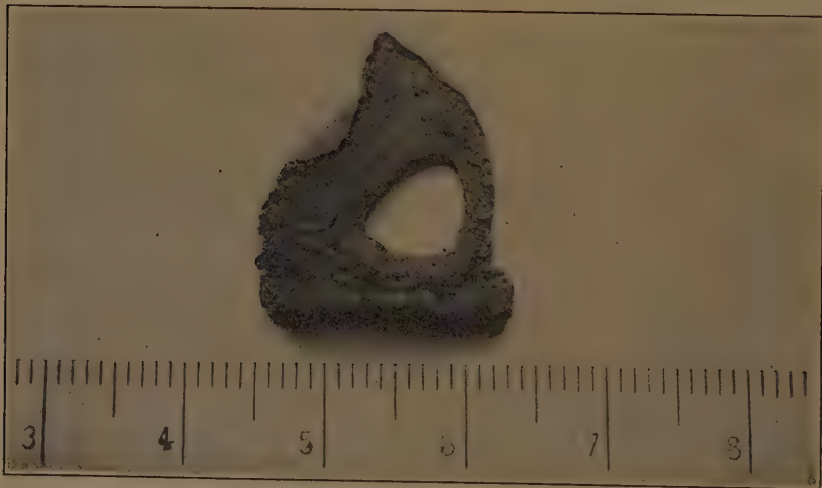


FIG. 52.—CYST OF SPLEEN. (Courtesy of Dr. W. G. MacCallum.)

Theories as to Origin.—Beneke's observations led him to believe that the formation of these cysts is dependent upon minute ruptures of the capsule with protrusion of spleen pulp. In the process of repair, he believes that inclusion of peritoneal cells takes place and leads to the peritoneal "epithelial" lined cysts. (Epithelial is here used as synonymous with peritoneal.) The ruptures of the spleen he attributes to sudden intense congestion. Ramdohr agrees with this. Ranggli explains these multiple cysts as infolding of peritoneum as a result of superficial inflammation.

Pepere believes that all these small cystic excavations have their origin from subcapsular cell-nests or strands of "epithelial" cells, which

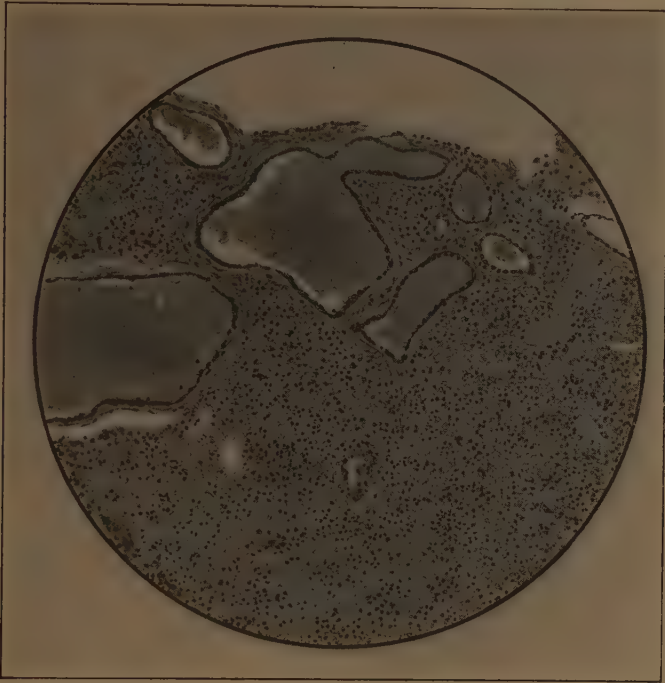


FIG. 53.—SMALL MULTIPLE CYSTS OF SPLEEN.
Autopsy specimen.

are derived from abnormal depressions of the perisplenium and its serosa, or from an incomplete fusion of the connective tissue and epithelial layers on the floor of the fissure, during the development of the growing organ.

Schmidt interpreted the cysts as due to capsular ruptures with dilatation of preformed canals, probably of lymph vessels of the capsule and trabeculae. He recognized that the existence of such lymph vessels in man had not been established, but believed they existed.

P. C. Potter did some experiments for us in the Surgical Research Laboratory of Columbia University in an effort to determine the nature of the lining cells of spleen cysts. Cysts were produced in the spleens of dogs by the implantation of celloidin balls. In 2 cases, the celloidin

spheres were surrounded by omentum. From two to three weeks later the omentum was ligated and cut, the object being to secure a peritoneal lining for the cyst. In all the experiments, irrespective of whether omentum was implanted or not, a connective tissue cyst wall was found when the spleens were removed and the cysts sectioned. This lining was similar to the walls of hemorrhagic cysts such as that described by Lambert.

The type of experiment was as follows:

Dog 1,958, March 29, 1921.

Procedure.—Incision ($1\frac{1}{2}$ cm.) made in anterosuperior border of spleen. Small cavity produced with curette. Ball of celloidin ($\frac{1}{2}$ cm.

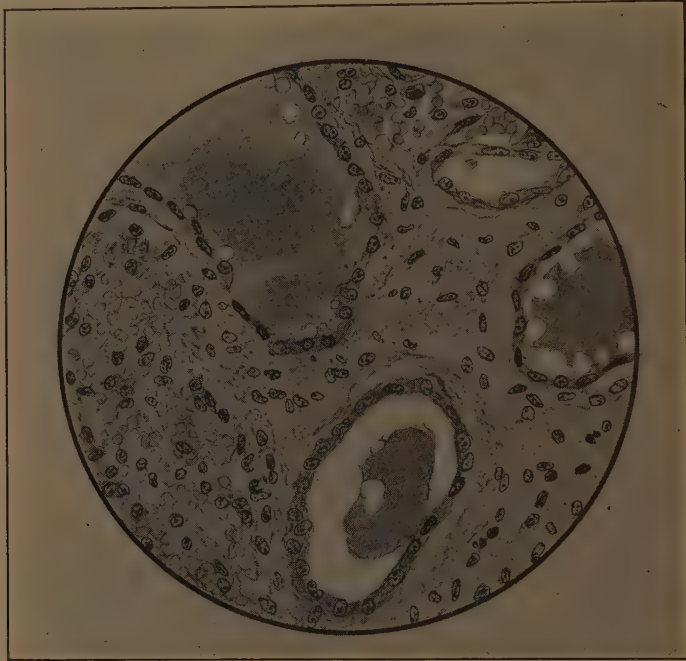


FIG. 54.—HIGH POWER OF PRECEDING ILLUSTRATION TO SHOW CHARACTER OF LINING CELLS.

diameter) wrapped in omentum introduced. Wound in spleen closed about omental pedicle with silk suture. Spleen returned to abdomen.

April 15, omental pedicle ligated and cut close to spleen. May 31, 1921, spleen removed. Sections cut.

Gross. There is a cystic cavity lined by a definite wall (Fig. LVI).

Micros. The wall is composed of firmly arranged cells which were interpreted as connective tissue, the inner surface of which shows flattened connective tissue cells with here and there collections of cells which are more globular in form with larger and more deeply staining nuclei.

Summary.—The origin of these small cysts has not been definitely estab-

lished. It has not been proved that they are of peritoneal origin, either as infoldings or cellular rests. The histological appearance of the lining cells is not conclusive of this interpretation and other convincing evidence

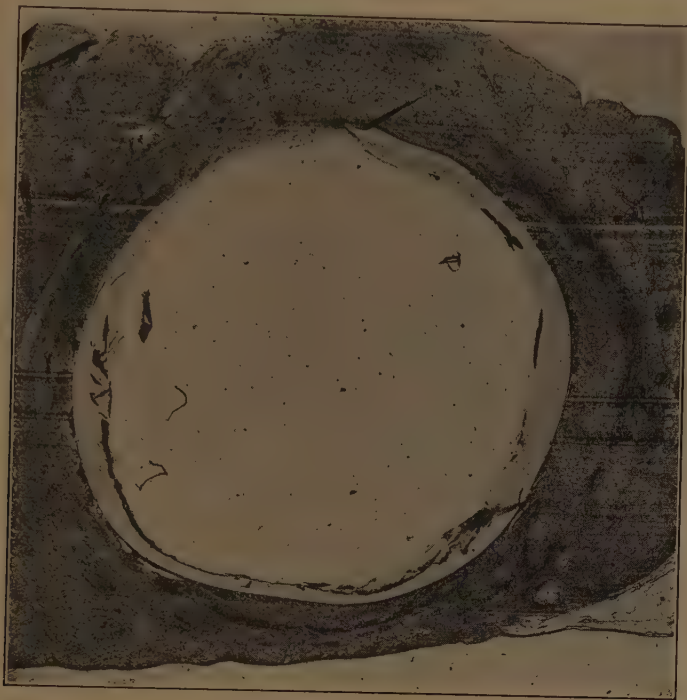


FIG. 55.—CYST OF SPLEEN IN DOG.
Produced by implantation of celloidin ball surrounded by omentum.

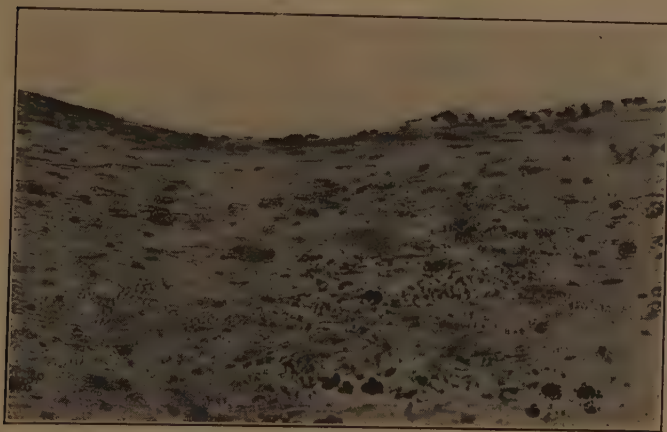


FIG. 56.—WALL OF CYST OF PRECEDING FIGURE.

appears lacking. The fact that these cysts occur in the anterior margin suggests some anatomical peculiarity or some external factor which affects this area. The obvious suggestive features are that lymphatics

are more numerous in this region of the spleen and that the cysts are lymphatic dilatations. But little is known of the splenic lymphatics and nothing can be said of this assumption except that the histologic structure of the cysts is consistent with the theory that they are of lymphatic origin. Nor can weight be given to the traumatic hypothesis, since other portions of the spleen are equally exposed to trauma.

Polycystic Spleen or General Lymphangiectasis.—Multiple multilocular cysts were attributed to the lymphatic system by Fink. This explanation is held by Kühne and Schmidt. The lymphangiectasis has been explained by mechanical factors, also as the result of inflammatory

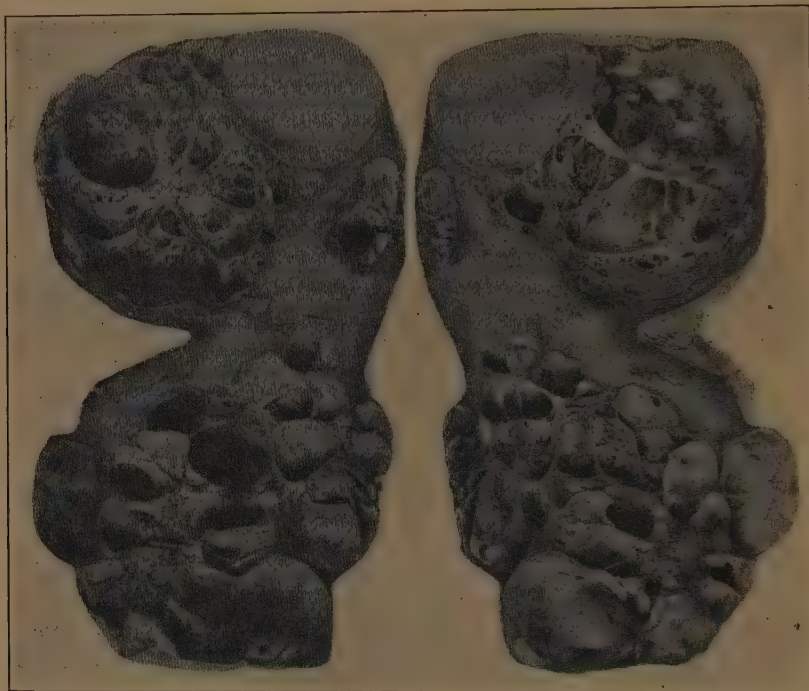


FIG. 57.—POLYCYSTIC DEGENERATION OF THE SPLEEN. (Courtesy of Dr. R. H. Fowler, *Annals of Surgery*.)

processes, but the cause is really hypothetical. The size of the organ may be considerably increased.

Coenen explained his case of multiple small cysts as general lymphangiectasis of the spleen and refers to it as polycystic degeneration of the spleen.

Apparently localized dilatations of lymph vessels, which by some have been interpreted as lymphangiomata, occur as in the case summarized below. Possibly this is the precursor of a general lymphangiectasis.

Male, twenty-five years old. Bellevue Accession No. 592. Pneumonia, lobar; fatty infiltration of liver; cysts of spleen. Died December 21, 1905.

Spleen showed along the anterior margin a number of cysts, the largest about the size of a pea. These appeared to be principally in the capsule, but on section, extended a short distance into the parenchyma. Otherwise the spleen was firm and showed no further change:

Dr. Muller, of the New York Hospital, described this tissue as follows: In the spleen directly beneath the capsule, there is a multilocular structure composed of about eight cavities in the section examined. These vary from $\frac{1}{2}$ to 2 mm. in diameter, and the whole group is 4 to 5 mm. in diameter. Directly beneath the capsule and attached to it is a series of four minute similar cavities from pin point to 1 mm. in size. These latter extend for a distance of 7 mm. to one side of the main cavernous structure. All these spaces are filled with a pink staining, shiny, homogeneous material resembling coagulated lymph. In it are a few isolated large mononuclear cells, with clear, pale cytoplasm and a small round nucleus. A few red blood-cells are also present in this homogeneous material. In some cavities, this red material has a very finely reticulated structure. The walls of these cavities consist of hyaline connective tissue. Where a cavity is directly beneath the capsule, the capsule itself is continuous with the rest of the wall. Where the wall separating two cavities is wide, there is found splenic tissue in this wall; but a narrow partition between two cavities consists only of hyaline connective tissue. The cavities are lined by a single layer of slightly flattened large cells, having large, round or slightly oval, nuclei and clear cytoplasm. The cells found free in the cavities suggest exfoliated lining cells. The entire structure resembles a lymphangioma of a cavernous type.

Dermoid Cyst.—Andral reported a case in which a cyst presented a fibrous wall and contained a greasy material in the center of which were disseminated some hairs. Kumaris, in 1915, reported a definite case of dermoid.

Symptoms.—No summary can be given which will present the clinical picture of cysts of the spleen. The involvement of the spleen, even with extensive destruction of its substance, causes no symptoms. Symptoms are due entirely to extraneous causes, adhesions and pressure. The growth of splenic cysts is usually very slow, extending over several years. The general condition remains unaffected, although the cyst may reach an enormous size.

The patient usually complains, if at all, of intermittent attacks of pain or continuous discomfort and dragging in the left hypochondrium or epigastrium. Digestive disturbances, especially nausea, flatulence and constipation, are frequent, while vomiting at times occurs due to pressure on the stomach. Other organs may be affected, especially if the spleen is displaced. Frequently the patient presents himself on account of a mass that has been noticed in the abdomen and has gradually increased in size.

The difficulty of diagnosis is emphasized by all writers. A cyst of the spleen cannot be recognized before it has attained considerable

size, especially when it occupies a deep position. The true condition is usually not recognized until operation has been undertaken for an unidentified abdominal tumor. Such features as dullness in the splenic region on percussion, movement with respiration and, in rare cases, fluctuation may lead to a correct diagnosis.

That the prognosis is good in spite of occasional rupture or suppuration is shown by the analysis of compilations of cases, for instance Carsten's list of 22 cases with 1 death.

Treatment of Cysts of Spleen.—Small multiple cysts do not demand surgical intervention. Polycystic degeneration indicates splenectomy. The large single cysts are the type which usually are encountered and alone demand discussion. The operative procedures which have been performed for this type are splenectomy, incision and drainage, marsupialization, extirpation of the cyst, and tapping with or without injection of antiseptics.

Splenectomy has been performed in approximately one-half of the reported cases. This procedure is especially indicated when the splenic tissue is to a large degree destroyed, or when the cyst is developing in a displaced or considerably enlarged spleen. Splenectomy is the ideal procedure and should be employed if adhesions are not firm. The spleen tissue is usually largely destroyed by compression and therefore it is useless to attempt to preserve the organ. The operation avoids the disadvantages of drainage and resection and effects a speedy cure. Of the 10 cases reported by Powers, all recovered. Maples' case of splenic cyst, in an African bush woman about forty years of age, is of special interest in view of the large size of the cyst, which so completely filled the abdomen that a diagnosis of ovarian cyst was considered probable. On account of the freedom of the spleen from adhesions, splenectomy was performed and was followed by uninterrupted recovery.

Incision and drainage of the cyst requires a protracted after-treatment, and should be reserved for large cysts in which the spleen is firmly adherent to the surroundings, making splenectomy impracticable or unduly dangerous. Powers reports 3 recoveries, 1 fistula and 1 death from sepsis. Marsupialization is the operation of choice in the presence of firm adhesions, but the persistent fistula not infrequently causes a protracted convalescence. Solieri, finding it impossible to do a splenectomy on account of the dense adhesions, was forced to marsupialize the cyst. A fistula persisted for six months. In Heurtaux's case, a fistula persisted ten months. Yet a fistula is not an invariable sequel. Huntington treated successfully by marsupialization a cyst containing two gallons. Other similar results have been reported.

Many operators have elected *resection*, or *enucleation* of the cyst. But this procedure is often technically difficult unless the cyst lies immediately under the splenic capsule. Hemorrhage is often profuse, but as a rule may be controlled by suture or packing. Johnston and others have successfully shelled out a cyst and closed the area with sutures.

Puncture of cysts is probably useless, as they may be expected to refill. Tapping of the cyst and injection of antiseptics was practiced in 8 recorded cases; 2 died of peritonitis. As Michelsson emphasizes, the procedure is unwarranted.

Echinococcus Cyst.—*Echinococcus* cyst of the spleen is rare. Thomas' analysis showed that only 2 per cent of cases of *echinococcus* cysts involved the spleen. He found the spleen affected in 88 cases, and in 45 of these the spleen was exclusively involved. Vegas and Cranwell reported the spleen involved in 3.15 per cent of 952 cases. Others confirm these figures. It is impossible to explain the entrance of the embryos into the spleen. Ordinarily they enter the portal vein and are conveyed to the liver; however, it may be inferred that they reach the spleen through venous channels.

Michelsson states that, although the parasite may lodge in any part of the spleen, its site of predilection is in the center, and the growing cyst in such cases separates the poles, with the result that the spleen assumes an elongated shape, which, by some, is considered characteristic of *echinococcus* disease of the spleen. The enlargement generally reaches considerable size. Adhesions usually form early between the cyst and adjacent organs, especially the diaphragm, liver, stomach, omentum, intestines or pancreas.

In some cases, the cyst has ruptured and the disease has become disseminated. Not infrequently suppuration occurs, in which case there ensue local and general evidences of sepsis.

Most of the cases have been recognized in adult life between twenty and fifty years of age. The sexes have been affected about equally.

The symptoms depend largely upon mechanical factors: size, situation and rapidity of growth. Central cysts, as emphasized by Trinkler, cause fewer and later symptoms than those near the surface which give rise to pressure and adhesions, while the cyst is much smaller. The mass usually conforms roughly to the splenic area and moves with respiration. If the spleen is displaced, considerable confusion as to diagnosis is apt to arise; but the true condition may be suggested by the absence of the spleen in its normal position as evidenced by percussion and X-ray examination, the last aided by pneumoperitoneum. Fluctuation was found in 24 of 51 observations; hydatid thrill, only 8 times. That the hydatid thrill is not a frequent sign is indicated by the summary of Hagan who found in 122 cases of hydatid cysts of various organs only 15 instances where a positive thrill was demonstrable. Rolleston, in discussing cysts of the liver, states that the presence of the thrill is not absolute evidence but is strongly suggestive of hydatid cyst. Eosinophilia is usual unless the parasite has died, for instance as the result of suppuration. Considerable albuminuria was present in 2 of 3 cases of hydatid cyst operated upon by Martelli, and subsided after the operation, being apparently of toxic character, like the eosinophilia. The various specific tests such as complement fixation, cuta-

neous and precipitin reaction apparently are of uncertain value as diagnostic aids.

Exploratory puncture, as Rolleston emphasizes, should not be undertaken, inasmuch as serious symptoms and even death may follow the escape of a small quantity of fluid into the peritoneal cavity. Although as a rule no serious symptoms develop, intense itching followed by urticaria may result, lasting a few hours to several days; at times, peritonism follows tapping, and, in rare cases, death preceded by convulsions and collapse has occurred.

Chauffard cites the case of a man aged thirty-five years in whom a hydatid cyst was punctured and 10



FIG. 58.—ECHINOCOCCUS CYST. (Courtesy of Dr. J. M. Hitzrot.)



FIG. 59.—ECHINOCOCCUS CYST, OPENED (Courtesy of Dr. J. M. Hitzrot.)

c.c. of clear fluid drawn off. Epileptiform convulsions set in and death followed within twenty-five minutes. The cyst contained clear fluid which was without poisonous effect on animals.

The action of the poison contained in a hydatid cyst is discussed by Rolleston, Boinet and Chazoulière, Humphry and others in dealing with cysts of the liver. The bad effects of hydatid fluid are said to be due to anaphylaxis or hypersensitiveness and are comparable to those produced by the injection of a foreign protein or serum.

Fatal toxic symptoms supervened five days after abdominal operation and drainage of a hydatid cyst in a case recorded by Fuster and Godlewski. Besides the systemic disturbances, tapping exposes to the danger of disseminating the infection. Petit reported a case in which cysts developed in the abdominal wall after drainage.

The prognosis depends largely upon whether hydatid cysts are confined to the spleen or are multiple. If limited to the spleen, the disease is curable by operation. If rupture of the cyst or suppuration of its contents have occurred, the prognosis is less favorable.

Early operation is essential and removal of the spleen is indicated without aspiration for the reasons already given. After exposing the spleen, if it is necessary to diminish its size by aspiration, the peritoneal cavity should be carefully protected. Carstens collected 33 cases treated by splenectomy with 4 deaths. In 2, the result was unknown. Michelson puts the mortality at 17 per cent. He argues that this high rate is due to late operation, often for suppurative cysts, and that the operation in early uncomplicated cases should be almost devoid of danger. Excision of the cyst is not advisable, first, on account of the technical difficulties and, second, on account of the danger of opening the cyst with contamination of the peritoneal cavity. Drainage should be done only if splenectomy appears likely to rupture the cyst by reason of firm adhesions. In this case marsupialization should be elected. Treatment by aspiration alone should be condemned. This feature is emphasized because, as late as 1919, Cardarelli published favorable reports concerning this procedure.

Historical Note.—In 1829, Andral presented the first recorded case of cyst of the spleen. This was followed in 1838 by Livois who reported a case in which autopsy showed a large serosanguineous cyst. Leudet, 1853, presented a multilocular serous cyst before the Anatomical Society of Paris and stated that he knew of 4 or 5 similar cases. In 1867, Péan removed successfully a spleen for a cyst containing over three liters of serosanguineous fluid. Magdelain, in 1868, collected from the literature 14 cases of serous and hydatid cysts.

Koeberlé, in 1873, was the first to remove the spleen for hydatid cyst. The patient, a woman twenty-seven years of age, died seventeen hours after the operation. In 1881, a man forty-four years of age who suffered from a cyst of the spleen following an injury was operated upon by Credé with a favorable outcome.

Knowsley-Thornton, in 1884, performed splenectomy on a woman of nineteen years for cyst of the spleen; the organ weighed one pound and eleven ounces; the patient recovered. In 1886, v. Bergmann successfully performed splenectomy for hydatid cyst of the spleen on a woman thirty-eight years of age; and, in 1888, Fehleisen removed the hydatid spleen of a boy eleven years of age, with a favorable outcome.

Since that time reported cases have increased considerably in number. Among the conspicuous compilations may be mentioned those

of Jordan, 1903, who collected 11 simple cysts and 16 cases of splenic echinococcus cyst, adding a personal observation to each group. Carstens, 1905, collected 22 cases of simple cyst and 33 of echinococcus cyst of the spleen.

NEOPLASMS OF THE SPLEEN

As previously stated, the term "splenic tumor" was originally employed to designate any enlargement of the organ and therefore to include all varieties of splenomegaly. This was the prevailing usage during the early studies of the spleen. At a later date, the term "acute splenic tumor" was applied to the enlargements of the organ associated with acute infectious diseases. In recent years there has been a growing tendency, especially among surgeons and pathologists, to restrict the word "tumor" to neoplasms. Since these conflicting uses have resulted in confusion and ambiguity, it seems best to avoid altogether the term "splenic tumor" and to use the word "tumor" only when so qualified as to render its meaning unmistakable.

Consideration of the neoplasms which occur in any anatomical structure is usually based upon an analysis of those growths which are found or have been reported as occurring therein. In the case of the spleen, however, this method is unsatisfactory by reason of the small number of reported neoplasms, the negligible number of these which are available for comparative histologic study and the inconclusive published reports of many of the cases.

In view of these limitations, it is believed that a broader and clearer conception of this subject can be gained by an analysis of the theoretical neoplastic possibilities of the organ. This method of approach, moreover, simplifies the subject in that it concentrates upon the basic tissues from which the neoplasms take origin rather than presenting isolated types of neoplasms unclassified developmentally. On this basis, one is led to analyze as tumor progenitors the connective tissue framework, including the unstriped muscle fibers, and the cellular splenic tissue. Since there is normally in the spleen no epithelial element, epithelial growths can occur only as the result of embryonal rests and are strictly speaking not tumors of the spleen but tumors in the spleen. The relatively isolated anlage of the spleen would lead to the assumption that epithelial growths are likely to form only a very small proportion of splenic neoplasms. The rare instances of dermoid and other growths referable to fetal inclusions support this supposition. True epithelial growths, such as primary carcinoma, which could be explained only as originating in fetal inclusions, apparently have not been reported. The early reported cases of carcinoma must be thrown out for lack of microscopic confirmation.

Since the basic tissue for all varieties of connective tissue growths

is represented in the spleen, on theoretic grounds all forms of fibromata, angiomata, myomata, chondromata, and osteomata (metaplasia), might be expected to be found among the benign tumors; and spindle and round cell tumors of connective tissue origin among malignant growths. These theoretical conclusions are supported to a considerable degree by the analysis of published cases. There is no recognizable peculiarity in the connective tissue of the spleen which renders it more or less prone to neoplastic development than similar tissue elsewhere. That such tumors are relatively infrequent must be ascribed to some peculiarity in the organ which renders all primary tumors therein uncommon. But the occasional occurrence in the spleen of various types of connective tissue tumor should not excite surprise any more than their occurrence in other organs in which connective tissue elements are present.

The cellular lymphoid structure of the spleen renders it subject to the same neoplasms as originate in other lymphoid tissues. Thus, neoplasms similar to those which are encountered in the lymph-nodes are also found in the spleen. These embrace the various forms of lymphosarcoma, including the so-called endotheliomata. The unusual lesion, Gaucher's spleen, must be regarded rather as a systemic disease, than as a true neoplasm.

The natural history of all the enumerated growths is known, and there is no good reason for assuming that the course would be materially changed by their location in the spleen, except that quantitative differences in the rate of growth and tendency to dissemination of malignant growths might be expected on account of the vascularity and peculiar vascular arrangement of the organ. The fact that secondary or metastatic growths occur in the spleen less often than the vascular relations of the organ would lead one to expect, suggests some characteristic of this organ which might account as well for the infrequent incidence therein of primary tumors.

Sappington, in discussing metastatic growths of the spleen, quotes Mallory to the effect that in the last twenty-five years in 4,265 autopsies, cancer metastases in the spleen were found only 10 times; also Adler, who found in 374 cases of primary pulmonary carcinoma, liver metastases in 103, kidney in 58, brain in 53 and spleen in 18. He states that the rarity of splenic cancer has given rise to a supposition that the organ possesses a relative immunity to neoplastic development. Sappington, however, calls attention to the fact that neoplasms implanted in the spleen grow as well as in other parts of the body. He further emphasizes the significant fact, observed by Deelman, that metastatic splenic cancer occurs much more frequently than macroscopic observation would lead one to suppose. Deelman examined the spleen in 75 cases of carcinoma, and, in 7, microscopic splenic carcinoma was found although in not one of these was a metastasis recognizable by the unaided eye.

The consideration of splenic tumors would occasion little confusion

or discussion were it not that the lymphatic structure of the spleen, like that of the lymph-nodes, often renders it difficult to differentiate neoplastic from inflammatory or other enlargements. For the same reason, difficulty often arises in classifying undoubted neoplasms, notably the sarcoma. It is in connection with this type of neoplasm that most of the confusion has occurred and until tissue from a considerable number of cases can be assembled and studied, a satisfactory classification of sarcoma of the spleen cannot be made. To make possible such comparative histological studies, a system for the interchange of laboratory specimens should be established both at home and abroad through a central bureau. Only in this way can facts be expeditiously collected in regard to such unusual lesions. However, in the absence of these ideal conditions, the essential details of recorded cases will be reviewed.

Benign growths, exclusive of cysts, have been reported in rare instances and are said to include fibromata, enchondromata, osteomata, myxomata, lipomata, angiomata and lymphangiomata (Chavannaz and Guyot). Foà mentions fibroma, chondroma and osteoma. References, however, are not given, and Michélssohn mentions fibroma only. We have found few recorded cases of benign growths. Willigk reported a fibroma of the spleen in a man of fifty-two. In the parenchyma, there were several nodules partially calcified. The nodules were composed of dense, partially concentric, partially irregular, connective tissue bundles. Foà described a tumor the size of an orange, having a definite boundary from the splenic tissue; it was classified as a nodular hyperplasia of the spleen or splenoma. Heinricius (1898) removed a large mass which apparently originated in the capsule of the spleen and was adherent to the omentum and intestines. The attachment to the spleen was cartilaginous and the growth appeared at operation to be a fibroma. It proved, however, to be a fibrosarcoma with myxomatous changes in the periphery. It seems likely that this case has led to the inclusion of myxoma and chondroma in several classifications.

The benign tumors do not attain large size and occasion no symptoms or signs by which a diagnosis can be made. By reason of their rarity, it is not usual to consider them seriously as diagnostic possibilities. The reported cases have usually been noted incidentally at autopsy after having given no indication of their presence during life. Consequently, nothing as to their clinical characteristics can be presented. The risk of enucleation of a supposedly benign growth is considerable, apart from technical difficulties, since a sarcoma which may be present as a circumscribed encapsulated mass may readily be mistaken for a benign lesion. Such was the experience of Heinricius. The relative harmlessness of removal of the spleen therefore indicates splenectomy in this type of case.

Under primary malignant tumors, there have usually been included sarcoma, angioma and endothelioma. Endothelioma is subject to some discussion and has been considered under Gaucher's splenomegaly and

lymphosarcoma; malignant angioma has been reported in a few instances and demands some discussion; while sarcoma, the most important and frequent malignant growth, must be considered at length.

Sarcoma.—According to Bush, there had been reported up to 1910 24 undoubted cases of sarcoma of the spleen. Of these, 11 were discovered at autopsy. The earliest case was probably that of Weichselbaum, in 1881, although Friedreich, 1865, reported a case which is accepted by some authorities, including Weichselbaum and Bunting. Jepson and Albert (1904) collected 32 cases, but some of these are doubtful by reason of indefinite histologic data. Among the cases reported since their publication may be mentioned those of Council, Power, Hendon, Mayo, Bush, Hauptmann, Meyer and Asch. It is not feasible to give a complete list, nor would the attempt be of any particular value. Sufficient has been said to emphasize the infrequency of the lesion.

Classification.—We attempted to secure for study slides of reported cases of sarcoma but with very limited success. Analysis of case reports did not fill the deficiency, since the descriptions are often not such as to allow visualization of the real structure of tissue nor to determine exactly what cases are similar. We found instances in which the opinion of the man who made the published report has been altered after a review of the material. Since no single observer has had access to tissue from an appreciable number of cases, generalizations have been largely theoretical. Yet analyses of the reported cases suggest that primary sarcoma of the spleen may occur in three forms, namely: fibrosarcoma (spindle cell sarcoma or round celled sarcoma) probably developing from the stroma; lymphosarcoma, developing from the lymphoid tissue; and large cell [often termed endothelial] sarcoma, probably originating from the endothelial cells of the stroma along the trabeculae.

Jepson and Albert described a case of the rare spindle cell variety. Weichselbaum (1881) and Heinricius (1898) also reported fibrosarcomata.

A number of cases of lymphosarcoma have been reported but analysis of these shows the difficulty of accurately classifying them from the case reports. It is impossible to enumerate the reported cases, although lymphosarcoma appears to be the most frequent type. But, as Giffin¹ states, "pathologists agree that a positive diagnosis of sarcoma of the spleen is hazardous and when recurrence does not follow there is a possibility that the tumor was in reality a benign lymphoma. One patient in whom splenectomy was done at the Mayo Clinic for what was morphologically lymphosarcoma has remained well for seven years."

Bunting (1903) presented a careful study of the large cell type. He stated that his was the third indisputable case of this nature, Grohé and J. Weber having published cases almost identical histologically. At the end of this chapter are summarized illustrative case reports includ-

¹ Mayo Clinic, 1912, 444.

ing examples of the three varieties above-mentioned. But it must be recognized that types may occur which cannot be ascribed definitely to any of the three groups. We have recently seen such a case (Fig. LXI and LXII).

In general, it may be stated of sarcomas of the spleen that the growth may be diffuse and produce a symmetrical enlargement of the spleen with obliteration of the normal structure of the organ, or it may occur as one or more discreet masses. In the early stages, a single, evenly circumscribed and apparently encapsulated nodule may be present. In primary growths, other nodules are usually connected with the original focus in contradistinction to metastatic growths in which the



FIG. 60.—LYMPHOSARCOMA OF SPLEEN. (Mayo Clinic.)

nodules are usually multiple and independent. Adhesions to adjacent organs seem to develop quite early with extension by invasion of neighboring structures. Metastases, especially within the liver, are common but have not been invariably present in the reported cases. But whether metastases occur early or late cannot be stated.

Symptoms.—The clinical features of splenic sarcoma are splenomegaly, pain or discomfort, emaciation and loss of strength. Sarcoma of the spleen develops insidiously. The first clinical sign is often a mass in the left hypochondrium. This may suggest a diffuse, smooth splenic enlargement with a notched anterior border, or present an irregular surface, hard and nodular. Occasionally the mass is tender on pressure. As the spleen becomes enlarged, traction on the capsule, ligaments, and neighboring organs often gives rise to more or less discomfort and pain.

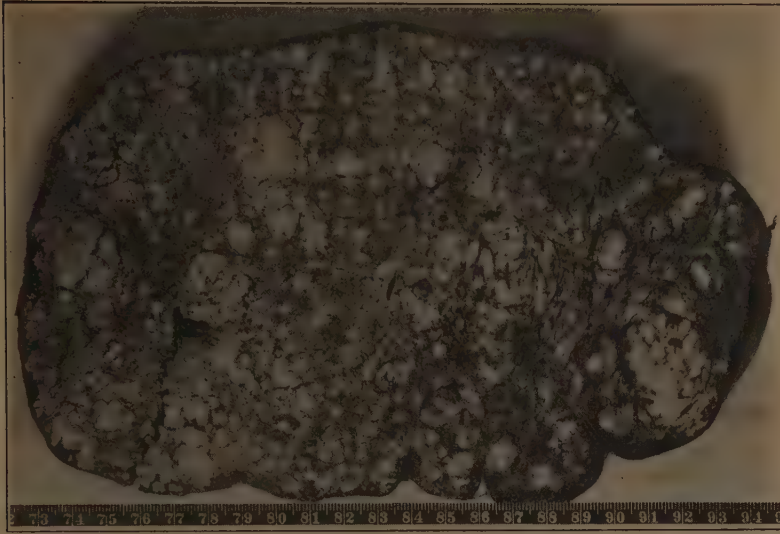


FIG. 61.—MULTIPLE LYMPHOCYTOMA OF SPLEEN. (Courtesy of Dr. J. M. Hitzrot.)

Spleen weighing 2,100 grams. On cut surface are seen white nodules from a few mm. to 2 cm. in diameter. Many are conglomerate. The splenic tissue between is small in amount and is depressed on cut surface.

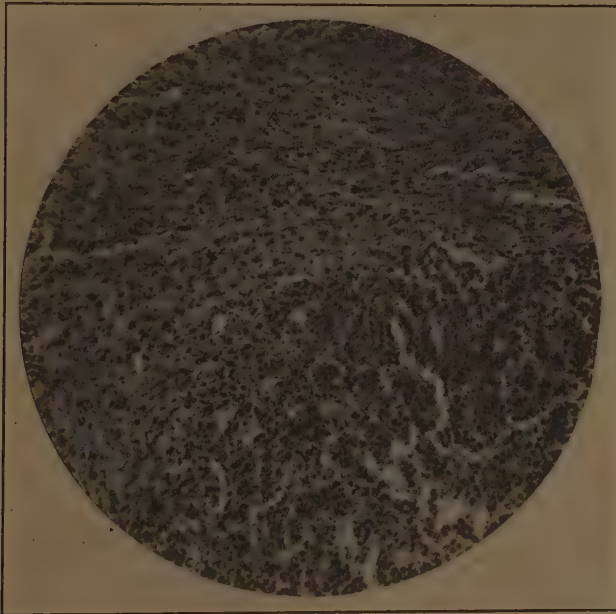


FIG. 62.—THE WHITE NODULES IN THE PRECEDING PHOTOGRAPH. (Courtesy of Dr. J. M. Hitzrot.)

They consist of collections of small lymphocytes. Between these foci are strands of spindle cells. Normal splenic tissue is not found. Dilated sinuses and considerable brown pigment in the form of granules are present.

Rapid increase in size, especially if there is irregularity of its surface, suggests primary sarcoma of the spleen. The growth never undergoes retrogressive changes, but presents a progressive increase in size. Blood examination affords no information indicative of the disease.

The enlarged spleen is friable and exposed, consequently it is prone to be ruptured by relatively slight external violence. Bush reported such a case in which intraperitoneal hemorrhage was severe and necessitated immediate operation. The colon usually lies below the tumor, but in Jepson and Albert's case it crossed the lower pole.

Treatment.—Early splenectomy represents the only therapeutic procedure which offers a reasonable chance of cure in malignant tumors of the spleen. Theoretically, in an early case of sarcoma of any type,



FIG. 63.—SARCOMA OF SPLEEN SHOWING EXTENSION OVER KIDNEY. (Courtesy of Prof. James Ewing.)

cure should be possible by operation since the organ is so easily removed. But this should be done by careful technic, using extreme gentleness with the least possible pressure upon the organ until the vessels have been ligated. If there is anywhere danger of disseminating tumor cells by rough handling of tissues, the spleen offers the ideal conditions. The only contra-indication to surgical interference is the existence of metastases or such weakened condition of the patient as to render operation impracticable.

The effects of radium and X-ray therapy cannot be stated. Such measures in the present state of development offer far less prospect of cure than does operation, and reliance upon them in early cases may cause the loss of valuable time. Yet the fact that lymphosarcoma of lymph-nodes is said to be susceptible to radiation encourages the em-

ployment of such measures when operation is unduly hazardous. In fact, there is some reason to believe that inoperable growths of this type may thus be brought within the field of operation.

The prognosis of sarcoma of the spleen is bad. Even the results of operative treatment are not encouraging, permanent cures being exceptional. Sarcoma usually leads to death within a year after the operation, as a result of recurrence or metastases. However, temporary improvement after the operation has frequently been noted. Therefore, splenectomy in malignant tumors of the spleen must be regarded as an operation which offers prospects of relief and occasionally of cure, and should be performed as early as possible. In Mayo's case of lymphosarcoma, the patient, a woman forty-one years old, was in good health three and a half years after the operation. Asch reported a similar result.

In Jepson and Albert's series of 32 cases (1904), 11 splenectomies were performed with 3 operative deaths; 3 patients died of recurrence, 1 was lost from observation, 1 was living six and a half years after operation (Fritsch, reported by Asch), 1 was well at the end of four years (Wagner, reported by Vanverts), 2 were living and well short periods after the operation (Jepson, Garré, reported by Simon). Finkelstein collected 33 cases of splenectomy for malignant tumors from the literature, with 7 deaths. Of Bush's collected series (1910), 13 cases were treated by splenectomy. There was an operative mortality of 4. He reported 4 patients as being alive sufficiently long after operation to warrant the possibility of cure. The others died of metastases or were lost from observation. It is disappointing that the late results of all such cases which have been reported once cannot be obtained. A satisfactory follow-up system will do much to give the individual surgeon information about his own cases. But more than this is necessary. The late results of previously published cases should be recorded when such cases are of types about which relatively little is known and about which much information is desired.

SUMMARIES OF SELECTED CASE REPORTS.—Jepson and Albert described a case of the rare spindle cell variety. The patient was a girl fifteen years old; a mass had been noticed in the left hypochondrium for five months and had gradually increased in size. It descended on standing, and on percussion the colon was found to pass in front of its lower pole, causing some confusion in the differential diagnosis between splenic or renal enlargement. Splenectomy was performed with uneventful recovery and six months after the operation the patient was apparently well. The mass weighed 256 gm. Its surface was nodular, hard, firm and dark purple red in color. The line of demarcation between the spleen and tumor was not easily distinguishable. The tumor consisted of round and spindle-shaped cells with large nuclei surrounded by a small amount of cytoplasm. There were dense white areas of fibrillar connective tissue containing only a few nuclei. The blood-vessels of the tumor were

poorly formed, most of them lined simply by endothelial cells; some contained tumor cells. A section of the specimen where the tumor bordered on the normal splenic tissue showed no distinct capsule but a crowding together of the normal elements for an area from 2 to 5 mm. in width.

In Grohé's case, the patient was a robust man of twenty years who had a fall after which he complained of pain in the region of the spleen. Symptoms of progressive anemia supervened, with weakness, digestive disturbances and headache. Three months after the accident, an enormous enlargement of the spleen was noted. Death occurred about six months later. Autopsy showed a large mass which included the enormously enlarged spleen as a whole and passed without definite boundaries into the liver and diaphragm. The bulk of the growth showed on cross section a number of grayish yellow transparent strands in a dark red, somewhat glassy tissue, producing a mottled appearance. A large segment towards the hilum consisted only of a gray opaque tumor tissue, interspersed with yellow areas. The consistence was hard in places, elsewhere soft; the lowermost portion of the spleen was adherent to the colon and omentum, and of much denser consistence; it contained not even a trace of blood-vessels. *Microscopically*, the mass consisted of fairly large round cells. The gray portions of the spleen presented no resemblance to the normal structure of the organ. There was no outline of pulp and malpighian bodies, the tissue consisting of rounded cells with large round nuclei. Between these cells, elongated spindle-shaped cells were seen, separately or in strands, but without forming a continuous tissue. A trabecular framework was nowhere demonstrable. In the macroscopically opaque yellowish areas, broad strands of connective tissue rich in nuclei were seen to surround islands of the above-described tumor tissue. The vicinity of the spleen was involved in the growth, so that the spleen, liver, omentum, and intestine formed a compact mass. The intestine presented individual disseminated nodules demonstrable in the serosa, precisely as in general carcinomatosis of the peritoneum. In other localities, the confluent nodules formed diffuse tumor masses. The liver was interspersed with metastatic tumors which formed large nodules. Besides these findings in the organs of the abdominal cavity, metastatic foci were found only in the right pleura, where small subpleural nodules were demonstrable. The spleen and liver contained many necrotic areas and numerous blood-vessels packed with streptococci.

Nordmann's observation concerned a woman of eighty-two years, whose spleen was said to be the seat of lymphosarcoma. The shape of the spleen was fairly well preserved, although its upper extremity was enlarged. On section, a firm round whitish central mass, the size of an orange, was found in the spleen, the white color contrasting sharply with the color of the organ. The tumor was composed of round cells supported by a fine stroma. The character of the tumor cells was the

same in the spleen and in the lymph-nodes, which presented numerous fibrous strands surrounding spaces filled with round cells.

Moppert recently reported a case which, on the basis of histological examination, was believed to be a lymphosarcoma. The patient, a man fifty-seven years of age, complained of pain in the left hypochondrium; the trouble dated back only six months; but the signs of great exhaustion were unmistakable, the patient having lost strength, appetite and sleep. The symptoms were referable chiefly to the stomach. On examination a mass the size of a fetal head was palpable in the left hypochondrium. After exclusion of all other possibilities, the diagnosis remained between syphilis of the spleen and lymphosarcoma. The patient was treated with X-rays and intravenous injections of neosalvarsan, but without beneficial effects. The mass increased in size and invaded the left flank in the form of hard irregular nodules. Ascites developed and death occurred three and a half months later. Partial autopsy showed 350 to 400 c.c. turbid fluid in peritoneal cavity, fibrinous exudate on peritoneum. The spleen, twice its normal size, presented at its lower pole a tumor the size of a child's fist. On section, it was found to be formed of a homogeneous whitish tissue extensively necrotic in the center. The upper pole of the spleen was intact, its tissue darkened and firm. The tumor of the lower pole was continuous at the level of the hilum with a thick layer of neoplastic retroperitoneal tissue which surrounded the (normal) left suprarenal body, reached the upper pole of the left kidney without invading it, encircled the aorta and the inferior vena cava, passed beyond the vertebral column, surrounded the right suprarenal and extended to the hilum of the liver. The pancreas was lost in the infiltration, but all its constituents were recognizable on section. The tumor had invaded the transverse mesocolon and then perforated into the peritoneum. All the other organs were normal. The tumor seemed to be derived from the spleen and to have invaded secondarily the retroperitoneal connective tissue.

Histological examination disclosed large round cells with distinctly basophile protoplasm. The outlines of the protoplasm were often irregular and slightly crenated. Sometimes an unstained perinuclear portion was seen in the cells. The nuclei were large and round, rich in chromatin, single, rarely double; and near the necrotic zones karyokinesis was demonstrable. At the boundary of the tumor and the spleen, necrotic zones with recent thrombi in the vessels were seen; around the vessels, neoplastic cells.

Kocher removed the greatly enlarged spleen of a woman, fifty-one years of age, who recovered after the operation. The excised organ weighed 3,530 gm. Kocher expressed a suspicion, although the histological findings brought no positive confirmation, that this tumor had the character of a malignant lymphoma or a lymphosarcoma, in view of the many small and large regional metastases which were seen at the operation and also in the specimen; also in view of the hepatic enlargement which failed to subside after the operation.

Herczel reports a case where the spleen was removed with a successful outcome, in a case of splenic sarcoma. The extirpated neoplasm was the size of a man's head. No metastases were seen in the abdominal cavity. The patient, a young man, was up eighteen days after the operation. Histological examination showed the tumor to consist of cellular elements barely exceeding the size of the white blood corpuscles and passing without a sharp boundary into the splenic parenchyma.

In Garré's case, as reported by Simon, a female, thirty-eight years old, since birth of her first child, eleven years previously, had had pain in upper abdomen but never so severe as to require medical attention. During the last (fourth) pregnancy rather severe pain developed in left upper abdomen. Normal delivery, normal puerperium. For five months pain still present but not so severe; no loss of weight. A smooth mass was felt in left hypochondrium; blood normal. Exploratory laparotomy; small amount of free fluid found. At the hilum were found some hard nodes closely applied and removed with spleen. When last seen one month after operation patient felt well.

Microscopic examination showed a round celled sarcoma with giant cells.

In Bush's case, a large celled sarcoma, the spleen weighed 2 pounds 14 ounces. It presented protuberances on the surface and nodules within the organ, the largest 7 cm. in diameter, the smallest 3 cm. Autopsy six months after splenectomy suggested that metastases had occurred by three channels: (1) through the blood stream to both lungs; (2) through the lymphatics to adjacent nodes; (3) by direct implantation on the peritoneal surfaces.

Bunting's case (1903) is one of the large cell type, in which the patient, a man forty-nine years of age, died in coma soon after admission to hospital. Postmortem examination revealed a spleen weighing 250 gm., slightly adherent. The cut section was uniform and of a peculiar purplish gray color. The liver presented numerous yellow nodules up to 10 cm. in diameter. Microscopic examination of the spleen showed slight thickening of the capsule and trabeculae. The normal structure of the pulp was entirely replaced by new growth. The new growth compressed the malpighian corpuscles on one side and the vessels of the pulp on the other. There was a delicate network of fibers forming pseudo-alveoli inclosing large oval, round or polygonal cells with finely granular or oval nuclei of variable size. Many of the cells showed mitotic figures and not a few were multinucleate. The average cell was somewhat larger than the large mononuclear of the blood. The blood-clots in the large veins and smaller sinuses showed tumor cells in number almost equal to that of the red blood corpuscles. Throughout the spleen were seen vessels apparently completely filled with these cells. The endothelium of the vessels seemed unaffected. In the liver, scarcely a lobule could be found in which tumor cells had not lodged and replaced liver cells. The portal vein and the capillaries of the lobules were engorged with tumor cells

of the type described in the spleen. In the connective tissue about the pancreas and once in the periphery of a lobule were found microscopic nodules reproducing the structure of the original spleen tumor. One enlarged lymph-node of the lesser omentum showed the sinuses throughout filled with large, actively proliferating tumor cells. In the subcutaneous fat were nodules partially encapsulated and made up of alveoli containing cells like those of the spleen tumor. Bunting states that the small size of the spleen growth in comparison with the metastases in the liver seems to be due to an early invasion of the splenic veins by the growth and the deportation of the elements to the liver which proved an effective filter. The invasion of the pancreas and lymph-nodes seems to have been by way of the lymphatics. According to Bunting, this was the third indisputable case of this nature, Grohé and J. Weber having published cases almost identical histologically.

Foix and Roemmele attribute the origin of these growths to the reticulum cells of the splenic follicles. The growth must be regarded as endothelioma, different from the Gaucher type which has been described elsewhere.

Angioma of the Spleen.—Cavernous angioma of the spleen, though rare, is of interest because the case reports excite discussion as to the possibility of malignancy in this type of growth.

Several authors have attempted to review the reported cases. Such analyses include those of Martin and Dowd. So few of these cases have been fully described that it is difficult to generalize in regard to the lesion. Yet a study of the reported cases, some of which will be cited, allows certain inferences to be drawn.

Jores reported the case of a woman forty-five years of age, in whom an enlargement of the spleen was noticed in December, 1906. In the spring of 1907, enlargement of the liver became demonstrable. The organ gradually increased in size. There were no blood changes except leukopenia. Death occurred in November, 1907, following edema and heart weakness. The spleen measured 31 by 15 by 16 cm. and weighed 3.60 kg. The surface was very uneven. On cross section, no spleen tissue was recognizable. There were many red gray, structureless masses, and one pole contained a blood-clot the size of a fist. The liver was enormously enlarged; on the surface were many nodules up to the size of an apple, of a purplish color and of fluctuating consistence. The masses showed no displacement of liver tissue. The spleen in places showed the typical structure of cavernous angioma. The remainder was necrotic, probably due, according to the observer, to intensive X-ray treatments. The liver lesion he considered as secondary, for the nodules in the liver were of irregular size and microscopically did not resemble a primary hepatic cavernous angioma. Jores reported the case as a sarcomatous angioma.

Langhans (1879) reported a similar case. The patient, a robust man of thirty years, had sudden pain in the splenic region, which followed

severe exertion. A pulsating tumor developed in the region of the spleen two and a half months later. At the end of a few weeks, the liver also became enlarged. The man died in four and a half months from exhaustion. The spleen measured 23 by 15 by 10 cm. The liver presented metastases. Microscopically both the liver and spleen showed the picture of a cavernous angioma.

In Dowd's case the patient, a well-nourished woman, aged thirty-seven years, for six months had suffered from pain in the splenic region. During a period of a week, two months before admission, she had suffered from repeated attacks of vomiting and epigastric pain, but there was no blood in vomitus or stools. For three weeks she had noticed a lump in the splenic region which had steadily increased in size. Its margin was round, its consistence firm; it moved with respiration. There was no clinical evidence of abnormality in other organs.

At operation the mass was found to be a greatly enlarged spleen, which was removed. It was adherent to the surrounding tissues, and a cyst containing about three pints of blood in the parenchyma of its upper end was ruptured in the operation. There was no lining membrane.

Microscopic examination of the spleen showed many blood spaces of large and small size. The stroma was scanty in places and elsewhere exceedingly dense and cellular. It was not possible to find any true splenic tissue, though in places there were small aggregations of round cells, suggesting lymphoid tissue. In a word, the bulk of the spleen was made up of blood-vessels and stroma and extravasated blood. The diagnosis was cavernous angioma of the spleen.

Immediate recovery from the operation was satisfactory. At the operation, many small dark cystlike spots were noticed on the under surface of the liver; they were about a quarter of an inch in diameter and were not elevated. The subsequent course led to the belief that metastases occurred. The liver became greatly enlarged, marked anemia developed, bloody fluid was aspirated from the chest. The patient died about three months after operation.

Homans reported a case of a woman of twenty-two years, who was tapped several times with removal of bloody ascitic fluid. A mass in connection with the omentum containing a supernumerary spleen was removed. There was no change in the accessory spleen, but the piece of omentum removed from the neighborhood of the colon showed angiomatous structure. Four months later, the spleen was removed and was found to present a cavernous angioma of the same character as that removed at the first operation.

In one of the cases reported by Theile, areas of spindle celled formation were found in the spleen, liver, lungs, and stomach. These were apparently sarcomatous. The spleen showed the characteristics of an angioma in general, but similar spindle celled formations were found.

The cases of Martin, v. Benckendorff and Anzilotti recovered after splenectomy; it is not known whether other organs were involved.

v. Benckendorff's patient was a patient of fifty-three years, who had had a palpable tumor in the abdomen for two years. Examination of the spleen after splenectomy showed the tumor to be rather sharply demarcated from the splenic tissue which was compressed and confined to the two poles. Ernst's case was one of multiple angiomas chiefly of the skin, but also of the liver and spleen. This case, however, cannot be included with the primary angiomas of the spleen.

Other cases, such as those of Albrecht and three of Theile reported from autopsies, add nothing of note.

The distinction between angioma and sarcoma of the spleen is not clearly marked either in the case reports or the classical discussions of these lesions. For instance, Theile considers hemangioma and sarcoma together. Theile states that in 1,900 autopsies covering a period of four and a half years, Lubarsch found 4 cases of sarcomatous angioma of the spleen.

From a study of the cases, there is no doubt that true angioma of the spleen, localized and benign, occasionally occurs. Such cases have been recognized at autopsy. Theile believed that a portion of the tumors, described as fibroma and fibrosarcoma by the older authors, were obliterated angiomas. Since cavernous consist of endothelial cells and stroma, either element may undergo malignant transformation with resulting sarcoma (Theile's case) or endothelioma. Metastases from such a neoplasm might be expected to present a vascular but not a cavernous structure, since the tumor cells cannot be supposed to exercise such control as would perpetuate the cavernous element of the parent growth. Finally the question arises as to whether a cavernous angioma as such may be malignant in the sense of exciting metastases. The reason for dwelling upon this factor is dependent upon the fact that several case reports imply or state that such is true. In this connection, we may analyze the cases tabulated by Dowd. Of the 13 diagnosed as cavernous angioma of the spleen, involvement of other organs was demonstrated in 5. In 1 of these (Theile), the metastases were evidently sarcomatous; in 1 (Ernst), congenital multiple angiomas (simplex) occurred in the skin, liver and spleen; in 1 (Homans), a growth cavernous in character was found in omentum which may have been a local extension; only 2 (Langhans, Jones) showed nodules of cavernous structure in the liver.

With reference to these cases, even if angiomas are present in several organs or tissues, it is not conclusive evidence that they are of metastatic distribution, since it is well known that angiomas are commonly multiple, as in Ernst's case in which the spleen was one of the structures involved. It is possible in multiple cavernous involving several systems, including the spleen, that the growths develop not as metastases from a parent tumor but coincidentally as the result of some more or less generalized abnormality of the vessels. Further, a cavernous angioma which evidently gives rise to metastases must be credited with

doing so as the result of malignant transformation unless this is excluded by careful and thorough histologic study of the tissues. Yet, however skeptical we may be, the possibility of metastases from a cavernous angioma as such cannot be disproved since eminent pathologists accept some cases as metastasizing cavernous angiomata (Borrmann, Ewing, Shennan).²

Clinical evidence such as emaciation, anemia and bloody fluid in the serous cavities cannot be accepted as proof of malignancy as in Dowd's case, in which death was supposed to result from hemorrhages from angiomata in the liver. The amount of blood in the spleen cyst, three pints in that case, is an index of what may result from rupture of such a cyst.

Of the 13 cases, without distinction between types, which were collected and reported by Dowd, 4 were discovered at autopsy. In none were metastases present; in the cases of Martin and Anzilotti, the patients were discharged as cured, but the late results were not reported; 3 patients died without operation; 3 after splenectomy, and the outcome of 1 splenectomy is not given. The analysis shows no unquestionable cures, yet the autopsy findings in several cases in which no metastases were found demonstrates the fact that some cases are amenable to surgical treatment and cure. These are the benign angiomata, and the possibility of malignant transformation indicates early removal of the spleen. When angiomata or metastases are present in other organs, operation can be of value only in so far as it prevents untoward local complications such as rupture and hemorrhage.

Aneurysm of the Splenic Artery.—Relatively little has been written upon aneurysm of the splenic artery and therefore a full discussion of the subject will be given and the published case reports will be summarized. Although it may seem that undue importance is directed to this subject, it appears wise in a work of this kind to assemble such material. We have found 22 reported cases, of which abstracts are given in this chapter. A study of these cases shows that certain generalities may be drawn which are of value from the standpoint of diagnosis and treatment.

Frequency of Occurrence.—V. Schrötter found among 19,300 autopsies in the Vienna Pathologico-Anatomical Institute, 220 aneurysms, including 4 of the splenic artery. E. Müller, in the Jena Pathological Institute, found that among 183 aneurysms in 10,360 autopsies performed in the period from 1865 to 1900, 9 concerned the splenic artery. According to the investigations of Bosdorff, among 93 aneurysms found in 3,108 autopsies on individuals past twenty years of age in the Kiel Pathological Institute in the period from 1873 to 1888, there were 7 aneurysms of the splenic artery. Emmerich utilized the autopsy material of the Munich Pathological Institute, and in 8,669 autopsies in the period from 1871 to 1888 found 58 aneurysms including only one of the splenic artery. Lebert, in 1865, compiled 104 aneurysms of the abdominal aorta

² Ewing, *Neoplastic Diseases*.

from the German, English, French and Italian literature, but found only 39 aneurysms of its branches, 10 of which concerned the splenic artery. Aneurysms of the splenic artery, according to Lang, are more frequent than aneurysms of the renal artery. Griebel found a number of scattered reports of aneurysms of the splenic artery, but the total does not exceed that of the renal aneurysms.

The *etiology* of aneurysm of the splenic artery is obscure. Compression or kinking of the vessel as the result of displacement of the spleen, especially of an enlarged spleen, may be suspected as acting as a contributory factor. The cause of the changes in the vessel wall is usually left doubtful in the available reports, neither the history nor the microscopic examination affording information. Binder's patient suffered from arteriosclerosis at a relatively early age. Mulley believes that past infections, such as rheumatism, typhoid fever, pyogenic infections, may exert an influence. He is inclined to refer the origin of the aneurysm in his case to the sequelae of an osteomyelitis from which the patient had suffered ten years previously.

The spleen itself is, as a rule, uniformly enlarged, smooth and without adhesions to the vicinity. Compression of splenic veins by the aneurysm may cause chronic congestion and increase in size of the organ. Histologically, the spleen shows hyperplasia of the pulp and thickening of the interstitial framework, probably due to circulatory disturbances.

It is possible for a false aneurysm to develop in the presence of a defect of the splenic vessels resulting from wounds, as illustrated by Griebel's observation. The factors which apparently exert an influence in the development of aneurysm here as in other vessels are traumatism, arteriosclerosis and infection.

Symptoms.—In the reported cases of aneurysm of the splenic artery, the spleen was more or less enlarged. The splenic artery being a vessel of small caliber, pulsation in a large-sized aneurysm can hardly be propagated in all directions, and is accordingly absent in most cases. An indistinct vascular bruit was noted on examination in only 2 of the reported cases. Severe abdominal pains represented the only symptom in 3 recent and carefully observed cases. In 2 of these, the pains were associated with occasional attacks of syncope, referred by Mulley to irritation of the solar plexus through pressure from the aneurysm.

In a number of the reported cases, the onset of the disease was insidious and the course latent, until, at the end of several years of vague disturbances, the patient complained of abdominal pains, especially on the left side. The spleen is found to be enlarged and at times a mass is palpable either independent of the spleen or fusing with it. Occasionally this mass presents pulsation, thrill or bruit.

Eichhorst, in his textbook of pathology of internal diseases, says that, in a case observed by Heppner, the pulsations of a tumor the size of an apple could be felt in the epigastric region. A woman fifty-six years of age, observed by West, died from hematemesis, after having suffered

from abdominal pains, flatulence and diarrhea. The autopsy showed old adhesions between the aneurysm of the splenic artery and the pancreas and stomach, the aneurysm having ruptured into the latter. The symptoms of aneurysm of the splenic artery are far from distinct and it is not surprising that the diagnosis has rarely if ever been rendered before operation.

Treatment.—When the existence of aneurysm of the splenic artery is suspected, exploration should be made. If an aneurysm is present, splenectomy with extirpation of the sac should follow. Delay may result in a fatal hemorrhage. Of the cases reported in the literature in which *surgical* interference was resorted to, 3 of the 4 recovered. Winkler's patient was cured by means of splenectomy and extirpation of the aneurysm (1903), and Mulley (1918) reported an equally successful result in a similar case.

CASE REPORTS—Osler. The patient was a man thirty years of age, who had been ill for several months. There was a deep-seated tumor in the left hypochondriac region, the dullness of which merged with that of the spleen. There was no pulsation, but a bruit was heard. The chief symptoms were severe epigastric pain, occasional hematemesis and hemorrhage from the bowel, which caused death. At autopsy, a tumor was found which occupied the left hypochondriac region, being situated between the stomach and the transverse colon. On section, it was seen to be an aneurysmal tumor, about the size of a coconut. On tracing the splenic artery, a probe passed directly from it into the sac. The artery was somewhat dilated at the site of rupture and presented an irregular deficiency of the wall, beyond which the vessel was thickened and ran into the wall of the sac. The proximal part of the artery was normal. The sac communicated with the transverse colon. The spleen was small and flattened, closely enveloping the sac.

A case of false traumatic aneurysm following rupture of the splenic vessels through a gunshot injury came under Griebel's observation. The patient, a soldier twenty-five years of age, was wounded by a projectile passing transversely through the left lower renal pole, the diaphragm, the left lower lobe of the lung, and the splenic pedicle. The splenic vessels were totally ruptured and a large false aneurysm developed. About seven weeks after the injury, operation was performed under the diagnosis of suppurating hematoma. The source of the hemorrhage could not be discovered on account of old blood-clots, but the spleen was suspected and removed. The patient died before the abdomen could be closed.

The formation of the false aneurysm in this case was believed to be due to agglutination of the neighboring organs, so that a hematoma was walled off. From this hematoma, a false aneurysm communicating with the vascular stumps of artery and vein gradually developed.

Mulley's patient was a woman twenty-eight years of age, who made a good recovery after splenectomy and extirpation of two aneurysms of

the splenic artery. There was a history of osteomyelitis of the right leg, ten years previously. An indistinct thrill in the left hypochondrium could be felt on palpation, and heard on auscultation. Operation revealed hydronephrosis of moderate degree. The spleen was enlarged and of a deep purplish color. Enormously congested veins were visible. Near the hilum were two pulsating isolated aneurysms of the splenic artery, one about the size of an apple, close to the hilum, connected with the smaller, the size of a pigeon's egg, by a short apparently normal intermediate segment.

An interesting case was reported by Villard and Murard, in 1912. The patient, a man thirty-three years of age, who had presented a tumor in the epigastrium for two months, with severe abdominal pains, was operated upon under the diagnosis of pancreatic cyst; a roundish dark colored tumor was seen at the level of the upper border of the pancreas, and weak pulsations could be felt. Exploratory puncture yielded fluid which suggested a cyst with hemorrhagic contents. The sac was opened and the profuse hemorrhage was controlled by clamps. The operation was terminated by marsupialization. The clamps were removed on the fifth day; the wound became infected. Profuse hemorrhages occurred and the patient died. The autopsy showed a greatly dilated and thickened splenic artery, having the diameter and thickness of the aorta, and filled with decomposing clots. The origin of the vessel from the celiac axis was normal. The lesion consisted in dilatation and hypertrophy limited to the middle segment of the splenic artery.

Winckler, in 1903, removed a spleen which was greatly enlarged as a result of aneurysm of the splenic artery, causing great distress to the patient, a woman twenty-five years of age. The hilum presented enormously dilated and thickened arteries, having nearly the size of pigeon's eggs. The vessels were ligated and the spleen was extirpated without difficulty. The patient recovered. The spleen weighed 450 gm. Aside from general tortuosity and diffuse dilatation of the main trunk of the artery, the branches presented three aneurysms. Each of the sacs was approximately spherical. The spleen showed chronic congestion, moderate hyperplasia of the pulp, and marked induration of the trabecular system.

An aneurysm of the splenic artery, occurring in a man forty-seven years of age, was discussed by Binder in 1913. The spleen in this case was found to be distinctly enlarged. The patient died from internal hemorrhage. The autopsy showed an aneurysm of the splenic artery, the size of a walnut, close to the hilum. The vessel was very tortuous and opened at the hilum into an irregular cavity, the ragged end of the arterial tube projecting into the sac. The artery was atheromatous. The primary aneurysmal sac had ruptured and a so-called spurious aneurysm had formed. Finally this gave way, leading to perforation into the abdominal cavity and fatal hemorrhage.

Beaussenat, in 1892, showed a diffuse aneurysm of the splenic artery

in a man fifty-four years of age with a malarial history of long standing. The patient died as the result of pylephlebitis. At the autopsy, the spleen was found to be enormously enlarged. The entrance orifices of the branches of the splenic artery were extremely dilated and rigid. From its origin at the celiac axis to its termination at the hilum of the spleen, the splenic artery measured 45 cm. The entire portion between the tail of the pancreas and the hilum of the spleen was the seat of a voluminous aneurysmal dilatation measuring 35 cm. in length. The two ends were cylindrical, and each presented a diverticulum the size of a hen's egg, which communicated with the arterial cavity through an orifice 6 mm. in diameter. A number of flattened atheromatous patches were demonstrable on the arterial walls. A very limited nonatheromatous region at the level of the tail of the pancreas was the seat of a dissecting aneurysm, extravasated blood being demonstrable between the intima and adventitia. The remainder of the splenic artery presented marked dilatation without thinning of the walls or atheromatous patches except at the level of the left gastro-epiploic artery where it contained a hard atheromatous concretion extending into both vessels, and continuous by its lower extremity with the aneurysmal portion of the splenic artery. The splenic vein was lengthened and thickened.

Goodheart (1889) reported a case of arteriovenous aneurysm of the splenic vessels, with thrombosis of mesenteric veins and localized acute colitis, in a woman forty-nine years of age. He surmised an aneurysmal dilatation of the splenic vein in view of the existence of a peculiar bruit over the region of the spleen, and at the autopsy this vessel at the hilum of the spleen was seen to be dilated into a cavity the size of a hen's egg, filled with laminated clot. On dissection, a valvular communication was found between the splenic artery and vein, about two inches from the origin of the latter. The whole length of the splenic vein was dilated and tortuous. The spleen weighed five ounces, had a thick capsule, and contained several white wedge-shaped infarcts. The observer had no explanation to offer as to the cause of the communication between the vessels.

A case of ruptured aneurysm of the splenic artery of obscure origin, in a woman twenty-six years of age, was discussed by Ahrens in 1892. The aneurysm affected the splenic artery in the pancreas and was the size of a hen's egg.

Death from rupture of an aneurysm of the splenic artery was observed by Ayer, in 1883, in a middle-aged woman. Dissection showed that the splenic artery had undergone aneurysmal dilatation.

Davidson (1884) presented a specimen of aneurysm of the splenic artery obtained from a patient who died of cancer of the esophagus. Just beyond the first division of the splenic artery was an aneurysm the size of a bean. At the next division was one the size of a pea, and at the next three divisions there were still smaller ones. There was no disease of the coats of the splenic artery, and the transverse portion of the aortic

arch showed only a moderate degree of atheroma. The spleen contained infarcts old and new.

Before the Pathological Society of London, in March, 1885, Samuel West showed an aneurysm of the splenic artery in a specimen derived from a man aged fifty-six who had died from hematemesis. The only diseased condition detected on physical examination was an enlargement of the liver. At autopsy, the stomach contained two pints of bright red blood and presented an ulcer on the lesser curvature; a small aneurysm projected through the thickened base of this ulcer, and from this the hemorrhage had occurred. In the resulting discussion, Barlow referred to a similar case in which a large ulcer was found in the stomach. The pancreas formed part of the floor of this ulcer, and in the middle was an aneurysm of the splenic artery, about the size of a pea, which had ruptured and given rise to fatal hemorrhage.

The description of a specimen of aneurysm of the splenic artery from the body of a man aged thirty-seven years, who died suddenly, is given by the Pathological Society of London.³ The specimen showed a sacculated aneurysm as large as an orange, about two inches from the origin of the splenic artery.

A remarkable case of aneurysm of the splenic artery which had ruptured into the splenic vein was reported by Weigert in 1886. The condition was discovered at the autopsy of a woman forty-nine years of age. A branch of the splenic artery presented another smaller aneurysm, and the splenic vein was enormously dilated, forming a sac over 11 cm. in diameter at the hilum of the spleen. This large sac at the peripheral end of the splenic vein protruded below under the tail of the pancreas, and a number of enlarged veins from the spleen opened into it at the left border of the sac. The trunk of the splenic artery had an average circumference of 1.6 cm. A branch of this artery, which led into the lower segment of the spleen suddenly became dilated at the hilum into a round sac with a diameter of 1.7 cm. This sac was very firmly connected below with the dilated peripheral portion of the splenic vein, and above presented a round orifice which led into another larger sac of oval configuration. At the left segment of this larger sac opened several not markedly dilated venous vessels from the spleen. From the right lower end, an oval orifice led into the above-mentioned greatly dilated segment of the trunk of the splenic vein, the sac contrasting sharply from the wide venous lumen. The wall of the large (venous) sac was somewhat thicker than the wall of the smaller (arterial) sac. At the upper end of the spleen, a smaller arterial branch presented a sharply outlined dilatation, the size of a pea, which had not ruptured. The aneurysmal change accordingly consisted of a small closed aneurysm on a branch of the splenic artery leading to the upper portion of the spleen, and a larger aneurysm on a main branch of this vessel. Whereas the smaller aneurysm had not ruptured, the larger one had broken through into

³ Tr. Path. Soc., London, 1885, 36:151.

the splenic vein, indicating a preliminary agglutination of the aneurysm to the venous wall which could be distinctly demonstrated in the unruptured segment. The portion of the vein which communicated directly with the aneurysm was not the main trunk, but one of its branches, as shown by the saccular outline of this portion, lying against the main trunk. The second sac communicating with the aneurysm was shown to be a venous structure by the venous branches which opened into it.

Taylor and Teacher reported 2 cases of aneurysm of the splenic artery in 1911. They also presented a large aneurysm of the splenic artery from the Museum of the Glasgow Royal Infirmary. The first case was an aneurysm occurring within the substance of the spleen in a boy of fourteen years who died from ulcerative endocarditis. The autopsy showed a greatly enlarged spleen with deep puckering of the surface and moderate perisplenitis. The spleen contained several large masses of laminated thrombus, enclosed in cavities with smooth walls, the cavities communicating with one another. The large mass was clearly an aneurysm and related to the branch of the splenic artery at the hilum. For the last part of its course, just before it was lost in the large aneurysm, the vessel was slightly tortuous and showed a very marked dilatation. The observers point out that the etiology of the aneurysms can only be a matter of conjecture, but that they were presumably of inflammatory origin. The spleen itself showed the changes of chronic venous congestion.

The second case concerned a woman forty-three years of age, at whose autopsy (following death from enteric fever) some aneurysmal dilatations of the trunk of the splenic artery were demonstrated. The vessel was distended with thrombus and showed aneurysmal dilatations. The first of them, about half an inch in diameter, was situated about three inches from the origin of the vessel, and there were three others of irregular sacculated form, situated close to the hilum of the spleen. The aneurysms contained firm red thrombus, with little indication of a laminated structure. On microscopic examination, the walls of the aneurysms were found to be fairly thick and very fibrous.

A case of aneurysm of the splenic artery, possibly the result of a rise of blood-pressure due to embolism, was reported in 1893 by Selter. At the autopsy of the woman thirty-one years of age, who died with symptoms of brain abscess, a saccular aneurysm of the splenic artery about 45 to 50 mm. in diameter was found, separated only by a thin layer of connective tissue from the internal surface of the spleen and the tail of the pancreas. In addition to this aneurysm, there were multiple embolisms of various organs, evidently referable to the existing disease of the mitral valves, whereas all signs of general vascular lesions were absent, so that it seems reasonable to interpret the aneurysm as a result of the embolism. Almost all the branches of the splenic artery after its bifurcation were obstructed with thrombi and the artery was torn straight across 50 mm. from the hilum. These

findings were interpreted as explaining the origin of the aneurysm; the sudden obliteration of the splenic branches through emboli necessarily leading to a considerable rise of blood-pressure in the arterial segments situated centrally from the embolus, with the result that the arterial wall was ruptured and an aneurysm was formed.

Grosser observed a patient with a superficial perforating gunshot wound on the left side. Repeated hemorrhage from the wound was controlled temporarily by packing. Nine weeks after the injury, the patient died as the result of a profuse hemorrhage. Autopsy revealed a ruptured aneurysm, about the size of a walnut, which protruded from the surface of the spleen into a granulating cavity nearly as large as a fist, situated between the diaphragm and the adherent spleen.

A case of aneurysm of the splenic artery, associated with echinococcus cyst of the liver, was presented by Girard in 1910. Splenectomy was successfully performed. The aneurysm was the size of a hen's egg.

Wesenberg, in 1912, reported a case of death from exsanguination during childbirth (patient thirty-two years of age). Autopsy showed an aneurysm of the splenic artery (5 by 5 cm.) situated at the splenic hilum with a distinct rupture.

In the same year, Villard and Murard reported the case of a man, aged fifty-three, who had presented a tumor in the epigastrium for two months. During two years he had had several sudden attacks of violent colicky pains; the last was twenty-four hours in duration. Examination revealed an epigastric tumor to the left of midline, smooth, rounded and solid in consistence. Under the diagnosis of cyst of the pancreas, laparotomy was performed and the mass was opened in spite of definite pulsation. The patient died as a result of secondary hemorrhage. Autopsy revealed at the upper border of the pancreas an aneurysm of the splenic artery.

Marshall, 1922, reported a case of traumatic aneurysm of the splenic artery. The patient, a woman of twenty-seven years, had injured herself while cleaning a revolver, the bullet passing through the liver and pancreas. Two months later, operation revealed a ruptured aneurysm of the splenic artery, the size of a pea, which was ligated. Extirpation of the spleen was not necessary, as sufficient anastomoses were present. About four months later the patient committed suicide.

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CHAPTER XIII

HISTORY OF SPLENECTOMY

A review of the early reported cases of splenectomy is of interest, since it indicates the class of cases which were treated surgically and emphasizes the high operative mortality. The difficulty in the recognition of those types of splenomegaly which might be benefited by operation and the high operative mortality explain the slow progress of splenic surgery.

An attempt will be made to present the evolution of splenectomy from the beginning. Although there has been careful consultation of original sources, no claim to completeness is made. The chronological arrangement meets with difficulties for the reason that numerous cases are not reported by the operator until several years after the intervention, or perhaps only incidentally referred to in a discussion of other cases. Dating from the nineties of the last century, the performance of this operation became a matter of such frequent occurrence as to render inadvisable the inclusion of splenectomies after 1890.

Apparently the first excision of the spleen mentioned in the literature dates back to 1549, reference to it being made in Fioravanti's *Del Tesoro della Vita Umana*.¹ The patient was a Greek woman, aged twenty-four. The operation is stated to have been performed by Zacarelli, a surgeon of Naples, assisted by Fioravanti of Bologna, for hypertrophy of the spleen from quartan fever. The entire organ was removed, and the wound closed by sutures. The patient recovered, the wound being completely healed in twenty-four days. The spleen weighed 1,340 gm.

Viard, a French surgeon at Gian, in 1581, is credited with having been the first to remove a prolapsed spleen. The patient was a man who had been wounded in the left side; he made a good recovery. Reference to this observation is made by Rousset.

The authenticity of these very early cases is more or less open to question. About 1600, a barber in Paris is said to have ligated and excised successfully the protruding portion of the spleen following a wound.² A Somersetshire surgeon, assisted by Turbeville, operated, in 1673, upon an English butcher who had stabbed himself in the left side causing protrusion of the spleen, omentum, and coils of intestines. The operation, consisting in excision of the spleen and part of

¹ Venetia, 1570, lii, Cap. 8.

² Ballonius *Opera Omnia*, Tome I, 183.

the omentum, with reduction of the intestines, is said not to have taken place until three days after the injury, but the outcome was favorable (see Timotheus Clarke). Purmann, in 1677, is credited by some bibliographers with having performed the first resection of the spleen, on a man who, in falling, had wounded himself with his knife, causing a prolapse of the omentum and spleen, and cutting off a small portion of the latter. Recovery after six weeks.

Nicolas Matthias, a German surgeon, in 1678, attended a man who had an incised wound in his left side, with partial protrusion of the spleen. The protruding portion was ligated. The spleen was removed by knife on the third day, and the bleeding staunched by styptics. The patient recovered in three weeks and was known to have survived six years.

Hannaus, in 1688, removed a segment of spleen the size of a hand in a case of prolapsed spleen due to a stab wound. The patient recovered and was well one year later. About 1700, Fantoni, of Turin, and Gerbezius operated upon a little girl, after an unsuccessful attempt at reduction of the protruding spleen. The organ was ligated and removed on the fourth day. The girl was living three years later. According to Fantoni, Ferrerius, in 1711, extirpated a suppurating spleen lying in a peritoneal abscess. The woman, thirty years of age, recovered.

John Ferguson, a surgeon at Strabane, Ireland, in 1734, observed a man who had been wounded in the left hypochondrium with a knife. The case is reported by him as follows: "I found the spleen out at the wound, twenty-four hours after he had received the wound. I made a ligature with a strong waxed thread and cut away three and one half ounces of the spleen." About six weeks later, the patient was well and followed his business without inconvenience.

Mr. Wilson, surgeon to Sir R. Rich's Dragoons, in 1743, operated upon a soldier with a penetrating abdominal wound and protrusion of the spleen. The patient had passed the night unattended on the battlefield; the prolapsed and inflamed spleen could not be reduced, and was cut off. Recovery ensued.

Dorsch, in 1797, ligated and removed more than one half of the spleen in the case of a man thirty-five years of age, who had received a knife wound between the ribs; a part of spleen one inch wide and five inches long protruded. The patient recovered and survived twenty-three years.

Reference to a partial splenectomy performed in 1875 on a youth of nineteen years, operator not stated, is made by Lenhossek. The patient presented an incised wound of the abdomen with protrusion of the spleen; the protruding portion was ligated and cut off; recovery followed and he was in good health three years later.

O'Brien, a naval surgeon, pupil of Sir Charles Bell, is credited with the successful performance of a total splenectomy in 1816 on a Mexican

thirty-nine years of age whose spleen had been exposed for two days as the result of a stab wound. The vessels were secured by ligature, and the spleen completely separated on the twentieth day. Recovery in forty-five days, when the patient remarked that he felt as well as ever. According to Krumbhaar, this apparently is the first case of extirpation of the spleen reported in America.

In May, 1826, W. B. Powell, of Kentucky, operated upon a man thirty-six years of age who had been stabbed in the left side between the tenth and eleventh ribs. Two inches of the spleen protruded; reduction proved unsuccessful, and the protruding part was ligated. Nine months later the patient enjoyed good health.

In the same year, 1826, Quittenbaum, in Rostock, Germany, removed the hypertrophied spleen (weight five pounds eight ounces) of a woman twenty-two years of age through an incision in the linea alba; she died six hours after the operation. One thick silk ligature was applied which at autopsy was found to embrace the tail of the pancreas.

MacDonnell, of Purneah, India, in 1836, operated upon a man aged thirty who had been gored by an ox. The protruding spleen was ligated and afterwards excised; the patient recovered in two months. A French surgeon, Berthet, in 1844, reported the case of a man who had received a knife wound in the left flank; the spleen protruded, became gangrenous, and was excised eight days later. The patient recovered, and survived more than thirteen years. The autopsy showed a remnant of spleen, the size of a hazelnut, adherent to the stomach wall.

Küchler, of Darmstadt, Germany, in 1855, was apparently the first operator who removed the spleen in an authentic case of malaria. The patient was a man of thirty-six years, with malarial hypertrophy of fourteen years' standing; seven ligatures were applied to the pedicle; the excised organ weighed three pounds. Death occurred four hours after the operation, due to hemorrhage from an untied branch of the splenic artery. This case gave rise to a controversy between the operator and Gustav Simon, who, on behalf of the Darmstadt Medical Society, raised the question as to the legitimacy of splenectomy in diseases of the organ and positively rejected the procedure. Later, the Dorpat Medical Faculty upheld the views of Küchler.

The first successful removal of an enlarged malarial spleen in modern times is to be credited to an American operator, G. Volney Dorsey, of Piqua, Ohio, assisted by Drs. Brownell and Ledom of Palestine, Ohio. The patient was a farmer aged forty years, with hypertrophy of the spleen from malaria. The operation was performed on September 2, 1855.

In the same year, J. Schulz, of Radom, Poland, operated upon a young Polish woman twenty-two years of age, who had been wounded between the ninth and tenth ribs and presented a protrusion of the spleen. A ligature was passed around the hilum and the spleen cut off. The wound healed in fourteen days and the patient recovered.

In October, 1862, Dr. Alston, a Confederate surgeon from Texas, applied a ligature in a case of protrusion of the entire spleen due to a gunshot wound in the left hypochondrium, and in a few days the spleen dropped off. The patient was up and about at the end of two weeks.

Péan, in Paris, on September 6, 1864, removed the spleen of a young woman twenty years of age, suffering from a unilocular serous cyst of the organ. An incision was made from the umbilicus to the pubes. The patient made a good recovery.

T. Spencer Wells, in 1865, removed the enlarged spleen of a woman aged thirty-four years, through an incision seven inches in length. Two arteries and twelve veins were tied. The spleen weighed six pounds and fifteen ounces. The patient died six days after the operation, apparently from sepsis.

In 1866, T. Bryant, of Guy's Hospital, removed a spleen of four pounds seven ounces from a young man twenty years of age, suffering from leukemia, who died from hemorrhage two hours after the operation.

Professor E. Koeberlé, of Strasburg, on September 21, 1867, removed the enormous spleen of a woman forty-two years of age, through an incision in the linea alba eight inches in length. The patient died as the result of hemorrhage. The excised spleen weighed seventeen pounds, eight ounces.

T. Bryant, assisted by Durham, on November 9, 1867, removed the spleen of a woman forty years of age; the organ was adherent to the diaphragm and weighed ten and a quarter pounds. The patient died fifteen minutes after the operation from hemorrhage.

In the case of an Arab, aged thirty-five years, who had received a knife wound in the hypochondrium, causing protrusion of a large portion of the spleen, M. Bazille, a military surgeon, on March 5, 1869, applied a ligature on the fourth day and cut off the protruding portion. The patient recovered in three weeks and remained free from functional disturbances.

The first splenectomy for echinococcus cyst was performed by Koeberlé, in 1873, upon a woman twenty-seven years of age, who died seventeen hours after the operation. The spleen weighed 1,300 gm. and contained four liters of fluid. In the same year, Heron Watson, in Edinburgh, removed the enlarged spleen (weight twelve pounds) of a man who for ten years had suffered from leukemia. An incision was made in the median line, two inches above and below the umbilicus. The pedicle was ligated in two halves by a strong double ligature. The patient succumbed to hemorrhage during the operation. Spencer Wells, in 1873, removed the spleen of a woman forty-two years of age who died at the end of seventy hours from sepsis. The organ weighed 7.5 kg.

Urbinate, in Italy, in 1874, removed the enlarged floating spleen of a woman who died from peritonitis four days after the operation. The

organ weighed 275 gm. The autopsy showed rotation of the stomach due to an enormous gas inflation. The splenic artery was atheromatous.

J. P. McCombs, in October, 1874, observed the case of a young negro twenty-two years of age who had been wounded with a pocketknife. A ligature was applied around the protruded spleen near the wound and afterwards the spleen was removed. The patient was up and about in four days, and twenty-six months after the operation he was in good health.

In 1875, Markham reported a case of excision of a portion of the spleen, with recovery. The patient was an Indian who had received a penetrating wound of the abdomen over the region of the spleen which was extruded to the extent of three fourths of its volume. About thirty-six hours after the infliction of the wound, a portion of the prolapsed spleen had already become gangrenous. The organ was almost entirely removed by making a section nearly on a plane with the surface of the abdomen. The hemorrhage was "appalling," but the patient recovered and was seen again in good condition about one year later.

Péan, in 1876, removed the enlarged spleen, weighing 2.5 kg., of a woman twenty-four years of age, who recovered after nineteen days and continued well three months later.

Simmons, in Sacramento, California, in 1877, extirpated the enlarged and adherent spleen of a man forty-three years of age, with leukemia of three years' standing. An incision was made in the linea alba, and the pedicle was ligated in sections. The excised spleen weighed seven pounds and two ounces. Although no considerable amount of blood was lost during the operation, the patient succumbed to hemorrhage at the end of two and a half hours. Martin, in Berlin, Germany, in the same year successfully extirpated the slightly enlarged floating spleen, which apparently caused severe pain, in the case of a woman thirty-one years of age, who made a good recovery after three weeks, although it is stated that in securing the pedicle by a silk thread, the ligature slipped and a hematoma resulted. The operation was performed in twenty-eight minutes. Fuchs, in 1877, extirpated the malarial spleen of a woman forty years of age, who died eighteen hours after the operation from peritonitis. The spleen weighed twelve pounds and thirteen ounces. Billroth, in Vienna, in 1877 and 1879, removed the spleens in two cases of leukemia, both with a fatal outcome. The first patient was a woman forty-five years of age, who died from hemorrhage due to slipping of a ligature four hours later. It was found that the tail of the pancreas had been wounded. The spleen weighed six pounds and nine ounces. The other patient succumbed within one hour after the splenectomy as the result of persistent hemorrhage from small blood-vessels in the adhesions. The spleen weighed eleven pounds and eleven ounces.

Langley Browne, an English surgeon, in 1877, operated upon a young man of twenty years suffering from leukemia, who died suddenly

from shock five hours after the removal of the spleen. The organ weighed eighteen pounds and eight ounces. In another case of leukemia, concerning a man thirty-seven years of age, splenectomy was performed by Arnison, in England, in 1878, and was followed by death from hemorrhage or shock in five hours. The operation lasted one hour and ten minutes; much delay was experienced in ligating small blood-vessels. The spleen weighed seven pounds and thirteen ounces. In the same year, Geissel, Essen, Germany, removed the spleen of a woman, thirty-nine years of age, suffering from leukemia; the organ weighed nine pounds and fifteen ounces. Death occurred from hemorrhage at the end of sixteen hours. Czerny, in Heidelberg, Germany, in 1878, extirpated the slightly enlarged floating spleen of a woman, about twenty-four years of age, who recovered after four weeks. The pedicle was ligatured *en masse*. In the course of the same year, this operator removed the spleen in a case of leukemia, the patient succumbing to hemorrhage a few hours after the operation. Another patient of Czerny, a boy of sixteen years, died from hemorrhage six hours after splenectomy. Fischer, in 1878, removed the enlarged and congested spleen of a woman, forty-four years of age, who died of peritonitis a few days later.

Langenbuch, in 1880, starts the long series of splenectomies performed during the eighties of the last century. His patient was a girl of sixteen years, with simple splenic hypertrophy, the enlarged organ filling three quarters of the abdominal cavity. She survived the operation only a few hours. A woman twenty-two years of age, operated upon by Franzolini in Italy in 1881, for hypertrophy and incipient leukemia, recovered after the splenectomy; the organ weighed over three pounds. Haward, in England in 1881, extirpated the enlarged spleen of a woman forty-nine years of age suffering from leukemia. The organ weighed seven pounds eight ounces. The patient died from shock in five or six hours.

Credé, in 1881, attempted to remove splenic cysts, in a case of hypertrophy and cystic degeneration of the spleen following injury, but was compelled to remove the entire organ. The patient, a man forty-four years of age, made a good recovery.

Trendelenburg, in 1882, tore the spleen during the removal of a retroperitoneal sarcoma, to which the tail of the pancreas was so solidly adherent that it had to be removed likewise, together with the entire spleen. The patient left the hospital about three weeks later, but died eight weeks after the operation.

Splenectomy for simple hypertrophy of the organ was performed by Spanton, in England in 1883, in the case of a woman forty-seven years of age, who died seven hours later. The extirpated spleen weighed eight and a half pounds. Gussenbauer, in 1883, extirpated the enlarged malarial spleen of a girl seventeen years of age, with malaria and cachexia, who died on the third day after the operation.

from peritonitis. The weight of the spleen was 1,650 gm. In the same year, 1883, v. Bergmann extirpated the malarial spleen of a woman sixty-three years of age, who died of shock at the end of thirty-two hours. Billroth, in 1884, extirpated the spleen of a woman forty-three years of age, for primary lymphosarcoma; the patient recovered, but the operation was followed six months later by recurrence and death. Knowsley-Thornton, in the same year (1884), operated upon a girl nineteen years of age, for cyst of the spleen; the extirpated organ weighed one pound and eleven ounces. The patient recovered and was discharged after sixty-four days. Another patient, a woman twenty-five years of age, died from hemorrhage five hours after the performance of splenectomy. Thomson, in 1884, successfully extirpated the cystic spleen of a young woman of nineteen years; the organ weighed 0.8 kg. Rydygier, in 1884, removed the enlarged spleen, weighing six pounds, in a case of leukemia in a woman thirty years of age, who died twenty-four hours after the operation of hemorrhage from the abdominal wound. A woman twenty-four years of age, operated upon by Terrier in June, 1884, for hypertrophy and leukemia, died twelve hours after the splenectomy from capillary hemorrhage into the peritoneal cavity; the spleen weighed thirteen pounds. Koeberlé, also in 1884, extirpated the greatly enlarged spleen of a woman forty-six years of age, on account of hypertrophy following intermittent fever. The patient died soon after the operation, during which much blood was lost. Younkin, in the same year, in this country, removed the slightly enlarged wandering spleen of a woman thirty-two years of age, who made a rapid recovery.

Splenectomy was performed by Roddick, in 1885, upon a man with an abdominal wound involving rupture of the spleen and laceration of a kidney; death occurred six hours after the operation.

Albert, in 1885, performed a splenectomy for floating spleen, with a successful outcome, on a woman thirty-four years of age. The wound healed in four weeks. The organ weighed 2,700 gm. Another floating spleen was removed by Donat, in 1885, from a woman twenty-five years of age, who recovered after four weeks and was found to be completely cured on reëxamination nine months later. Prochownik's patient, a woman forty-one years of age, who was operated upon in the same year (1885), likewise recovered after extirpation of an enlarged floating spleen.

Thornton, in April, 1886, lost a patient through internal hemorrhage following the performance of splenectomy. In May of the same year, Polk, in this country, removed the displaced spleen of a woman who made a good recovery. In 1886, splenectomy was performed by Nilsen, with a successful outcome upon a woman with an enlarged floating spleen.

In May, 1886, McCann successfully removed the wandering spleen of a very anemic woman, twenty-nine years of age, who gradually

regained health and was well four weeks later. The spleen was extensively adherent to the omentum. Ceci, in Italy, also in 1886, extirpated an enlarged movable spleen, with a successful outcome, in a girl seventeen years of age. The excised organ weighed 2,400 gm. Meyers, in October, 1886, successfully removed the enlarged suppurating malarial spleen, lying in a peritoneal abscess, of a woman forty-one years of age; the organ weighed seven pounds. The patient was enabled to leave the hospital three weeks later. In the same year, Podrez extirpated the enlarged malarial spleen, weighing 1,756 gm., of a woman thirty-six years of age, who recovered from the effects of the operation but died about one month later from nephritis. A splenectomy performed by Ribera, in Spain, in 1886, upon a boy ten years of age, suffering from enlarged spleen and ascites, was followed by death from shock on the following day. V. Bergmann, in 1886, performed splenectomy in a case of echinococcus cyst of the spleen in a woman, thirty-eight years of age, who recovered. Fehleisen performed a successful splenectomy for the same disease in 1888. In 1887, Severeanu successfully removed the enlarged floating spleen of a woman, forty years of age, who recovered after fourteen days. The organ weighed 985 gm. Riedel, in the same year, successfully extirpated the floating spleen of a woman who presented no change in the blood picture after the operation, and Spencer Wells performed splenectomy in the case of a woman, twenty-four years of age, with an enlarged floating spleen weighing four pounds. The patient recovered. Leonard, in 1887, operated with a successful outcome upon a woman, twenty-eight years of age, for enlarged floating spleen; the pedicle was tied in three portions and the organ removed; its weight amounted to 600 gm. Strong, also in 1887, performed splenectomy upon a patient with an enlarged leukemic spleen, which weighed over nine pounds; the patient died. Burckhardt, in 1887, performed splenectomy upon a woman, forty-seven years of age, with an enormous splenic enlargement. She died from hemorrhage fourteen hours after the operation; the spleen weighed over ten pounds. Fritsch successfully removed the spleen, which weighed two pounds, in a case of primary lymphosarcoma concerning a pregnant woman, thirty-one years of age. The blood picture remained normal. The pregnancy went to term, but the patient was delivered of a dead child. She lived nine years after the operation and finally died from organic heart disease. A woman fifty-one years of age, with lymphosarcoma of the spleen, was successfully operated upon by Kocher, in 1888; the excised spleen weighed 3,530 gm. Splenectomy for enlarged floating spleen, in the case of a woman forty years of age, was performed by McGraw in the same year, and was followed by recovery. The same operator also reported the case of a man, twenty-seven years of age, upon whom he performed splenectomy on account of enormous enlargement of the organ; the patient died two and a half hours later from hemorrhage. Durante, in Italy in the same year,

performed an unsuccessful splenectomy upon a young woman of twenty years for echinococcus cyst; and Más, a Spanish surgeon, also in 1888, extirpated the spleen in a case of echinococcus cyst in a woman, thirty-two years of age, who recovered at the end of three weeks. In the same year, Roswell Park in this country removed the enlarged spleen of a man forty-seven years of age in a case of leukemia; the organ weighed eight pounds. The patient died a few hours after the operation. Albert, also in 1888, lost a patient from hemorrhage forty hours after the performance of splenectomy. A patient operated upon by Hatch, in 1888, a woman thirty years of age, died on the evening of the splenectomy from hemorrhage and collapse. Wright's patient succumbed to hemorrhage thirty-six hours after splenectomy; the spleen weighed one and a half pounds and was extensively adherent to the diaphragm. D'Antona, in Italy in 1888, removed the enlarged floating spleen of a woman, thirty years of age, who made a good recovery. In the same year, this operator performed a successful splenectomy upon a man of thirty-one suffering from malaria; the patient died five months later from cerebrospinal meningitis. In 1889, D'Antona performed splenectomy upon a boy two and a half years of age whose extirpated spleen weighed one tenth the total weight of the body. The child recovered from the operation, but died five months later from tuberculous meningitis. Klinger's patient was operated upon, in 1889, on account of a stab wound in the left side, causing prolapse of the entire spleen; a ligature was applied and the spleen removed after about fourteen days; recovery. Burckhardt, in 1889, removed the spleen of a woman twenty-six years of age, who after temporary improvement died from marasmus eight months after the operation; the excised spleen weighed six pounds. Another patient with splenic pseudoleukemia, upon whom splenectomy was performed by Burckhardt, in 1889, likewise died after temporary improvement, about three months after the operation. Czerny, in 1889, successfully extirpated the enlarged spleen of a man, twenty-four years of age, suffering from primary splenic hypertrophy; the organ weighed 1,500 gm. The permanency of the cure could be ascertained five years after the splenectomy. Flothmann, in 1889, performed splenectomy upon a man of forty-four years with sarcoma of the spleen; death occurred from hemorrhage after fifty hours. The spleen weighed over four pounds. Gersuny, in 1889, demonstrated before the Vienna Gynecological Society an enlarged spleen weighing over four pounds, which had been removed from a woman, forty-two years of age, who recovered after the operation. Lawrence-Burke, in the same year, reported the removal of a tuberculous spleen weighing three pounds from a woman, twenty-seven years of age, who died about thirty-six hours after the operation.

The increasing frequency of splenectomy in recent years is shown by a review of case compilations. One of the earliest collections was made by Magdelain, in 1868, who in a monograph on serous cysts of

the spleen gave a history of extirpation of the spleen. In the Medical and Surgical History of the War of the Rebellion, Otis tabulates the recorded operations for the removal of the spleen. The total was 26 cases. An instructive table of 29 cases was contributed by Herbert Collier (1882), including 16 cases in which the spleen was removed for leukemia. Adelmann (1887) collected 54 cases of excision of the spleen, extending over a period of thirty years; 37 of these splenectomies were followed by death. A number of extirpations of the spleen, grouped according to the cause which led to the operation, can be found in Max Spandow's Inaugural Dissertation, *Die Milz-Exstirpation*, Berlin, 1889. In the same year, Nicolai Sokoloff, in Petrograd, collected from the international literature 65 cases of total splenectomy for various causes, with 24 recoveries and 41 deaths (63.07 per cent). Of 117 splenectomies compiled by G. Vulpius in 1893, 59 led to recovery (50.4 per cent) and 58 terminated in death (49.6 per cent). The number of recorded splenectomies was raised to 279 cases by J. Vanverts, in 1897. Bessel-Hagen compiled, up to the date of his publication (1900), 360 cases of extirpation of the spleen, not counting those cases in which the prolapsed spleen was removed following an injury to the abdominal wall. In these 360 cases, there were 138 deaths, a mortality of 38.3 per cent. M. Jordan, in 1903, based his paper on the indications and results of splenectomy in nearly 400 extirpations of the organ. A short but comprehensive history of splenectomy was offered in 1905 by J. H. Carstens, who succeeded in compiling 739 cases. An important contribution to the subject was made by G. B. Johnston, who collected 708 splenectomies with 514 recoveries and 194 deaths, a mortality of 27.4 per cent. The history of splenectomy is briefly reviewed in an article by E. B. Krumbhaar, 1915.

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CHAPTER XIV

OPERATIVE PROCEDURES

SPLENECTOMY

The possibility that the spleen plays some rôle in the resistance to infection and that after splenectomy the resistance of the individual is diminished has been discussed. Though this relationship has not been established as applicable to man, there is experimental evidence to throw considerable weight on the theory. The evidence is at least sufficient to indicate caution lest the spleen be sacrificed unnecessarily. But in view of the relatively innocuous effects of removal of the organ, no question should arise in those cases in which splenectomy is definitely indicated. The immediate dangers of the operation cannot, as a rule, be anticipated. Beyond the trifling risk which attends every celiotomy, the chief dangers associated with splenectomy are dependent upon such factors as the friability and degree of fixation of the organ, the condition of the patient and the type of disease. A small non-adherent spleen in a relatively healthy individual may be removed with little risk. This, however, is not the type of organ which usually demands removal. Most of the operations are undertaken for conditions associated with some degree of splenomegaly; in many of the cases, the organ is friable and the vessels are much enlarged; in many, adhesions are present and fix the organ more or less firmly to the diaphragm. These factors predispose to hemorrhage which may be of extreme degree. Finally, a large proportion of the patients are profoundly anemic and show other evidence of lack of resistance. In this type of case, operative shock is an immediate danger, and postoperative pneumonia is relatively frequent. Careful study of the general condition of the patient is essential and should include a complete physical examination especially of the heart, kidneys, lungs and blood. An estimate then should be made of the patient's operative resistance.

The degree of danger in any case is dependent upon the individual peculiarities and cannot be estimated by the percentage basis of any of the tables which have been collected. These, however, are of interest in showing, first, that the immediate mortality is not excessive and, second, that the mortality has steadily diminished as surgical technic and judgment have improved. But, as in any similar study, the operative mortality of reported cases does not give a true index of the operative

risk, because successful cases are reported to a larger degree than the unsuccessful.

Bessel-Hagen, in 1900, compiled 360 cases of extirpation of the spleen with a mortality of 38.3 per cent. Eight years later, George Ben Johnston collected and tabulated 708 operations of splenectomy with 514 recoveries and 194 deaths, a mortality of 27.4 per cent. In the period from 1900 to 1908, his records show 355 splenectomies with 289 recoveries and 66 deaths, a mortality of 18.5 per cent. Deducting from these figures the 113 splenectomies done for wounds of the organ, 242 extirpations of the spleen are left with only 32 deaths, or a mortality of 13.2 per cent. Apart from traumatic and leukemic cases, there were 235 cases with 27 deaths, or a mortality of 11.5 per cent. More recent reports from the Mayo Clinic by Giffin, in 1921, include 245 cases of splenectomy for various conditions with a mortality of 10.6 per cent.

A discussion as to the indications for and contra-indications to splenectomy has been gone into under each subdivision. These features are summarized under their respective headings as follows:

Movable or Wandering Spleen.—If symptoms develop referable to the spleen, operation is advisable; if torsion occurs, operation is imperative. Other procedures than splenectomy have been for the most part discarded.

Traumatic Lesions.—Subcutaneous and open wounds of the spleen demand exploration and, in general, splenectomy.

Abscess.—Splenectomy should be confined to those cases in which the organ can be removed without serious risk of peritoneal contamination.

Cysts.—Small multiple cysts do not demand intervention. Polycystic degeneration indicates splenectomy. In large single cysts, splenectomy should be employed unless adhesions are very firm. Incision and drainage require a protracted treatment and should be reserved for large cysts in which the spleen is firmly adherent. In echinococcus cysts, removal of the spleen is indicated without aspiration. Drainage should be done only if splenectomy appears likely to rupture the cyst by reason of firm adhesions.

Neoplasms.—The risk of enucleation of a supposedly benign tumor is considerable apart from technical difficulties, since an early sarcoma may readily be mistaken for a benign lesion. The relative harmlessness of removal of the spleen, therefore, as a rule, indicates splenectomy.

In malignant growths of the spleen, early splenectomy offers prospects of relief and occasionally results in cure.

Pernicious Anemia.—All discoverable septic foci should be eradicated when possible and the patient should receive graded transfusions of whole blood. When the condition of the patient is improved and his ability to initiate a remission established, the removal of the spleen is apt to result in improvement and prolong life.

Splenic Anemia, Including Banti's Disease.—In the early stages of the disease, the removal of the spleen results in a symptomatic cure which

may be permanent or may last for several years. In the late stages, the operation is much more dangerous and the results less satisfactory. Yet even here splenectomy may be followed by marked improvement and prolongation of life.

Von Jaksch's Anemia.—Patients should first be treated medically. If they do not improve, the removal of the spleen is indicated and usually results in amelioration of the anemia, if not in actual recovery from the disease. Transfusion is an important adjunct to the operation.

Hemolytic Icterus.—Splenectomy results in a symptomatic cure in practically all cases, unless they are of very long standing. Transfusion is often an important aid to the operation.

Gaucher's Disease.—The removal of the spleen does not cure Gaucher's disease, but it does give mechanical relief and often is followed by an improvement in the anemia. In some instances, the disease seems to have come to a standstill after the operation.

Syphilis.—If vigorous antisyphilitic treatment does not yield satisfactory results, the removal of the spleen may be advisable.

Tuberculosis.—Splenectomy is the only measure that offers relief in "primary" tuberculosis of the spleen. It is not indicated in the secondary form.

Malaria.—Splenectomy is indicated in those cases in which the large spleen is in itself a cause of marked discomfort. The operation has no influence upon the infection.

Leukemia.—The operative mortality of splenectomy in leukemia was formerly very high, and it was believed that the operation was absolutely contra-indicated. Recently the spleen has been removed in a number of chronic cases after being reduced in size by preliminary radium treatment. The Mayo Clinic has reported 29 such cases with 1 postoperative death. They are all instances of the myelogenous type of the disease. These patients are not cured, but their lives have been prolonged. Giffin states that the operation is advisable in the very chronic form of the disease with a very fibrous spleen and a not very high white cell count.

In chronic lymphatic leukemias there is no evidence to justify splenectomy.

Polycythemia.—It has generally been believed that the splenomegaly of polycythemia is purely spogenous and that splenectomy is contra-indicated.

Portal Thrombosis.—Splenectomy may result in some improvement by diminishing the amount of blood in the portal system. If the thrombus is limited to the splenic vein, the removal of the spleen is likely to result in symptomatic cure.

Gastric Hemorrhage of Splenic Origin.—It is possible that, as a result of pathological changes in the spleen, there may occur alterations in the blood which result in gastric hemorrhage which may be relieved by splenectomy, but such a hypothesis has little to support it.

Cirrhosis of the Liver.—Splenectomy may produce a symptomatic improvement and prolong life. It does not cure the disease. It is rarely indicated.

Kala-azar.—Splenectomy is indicated to relieve mechanical symptoms after thorough treatment with antimony.

Tropical Splenomegaly.—The removal of the enlarged spleen may be indicated in Egyptian and Colombian splenomegaly to relieve symptoms produced mechanically and to check the anemia.

Beriberi.—Splenectomy is not indicated.

Schistosomiasis.—Splenectomy has not been performed but might be expected to result in improvement of symptoms due to cirrhosis of the liver.

Hodgkin's Disease.—Splenectomy offers no hope of relief or cure in Hodgkin's disease. It is not indicated in leprosy, actinomycosis or amyloid degeneration of the spleen.

Rickets.—The removal of the spleen is not considered in the treatment of uncomplicated rickets. When the rickets is complicated with anemia, the condition generally corresponds to von Jaksch's anemia and the indications are the same as in that condition.

Technic.—While the operator must be thoroughly conversant with the normal anatomical relations of the spleen, especially to the pancreas and stomach, and must be familiar with its peritoneal attachments and the situation and course of its vessels, it must be recognized that the conditions which are encountered in operations for enlarged spleens often differ considerably from the normal. There are often firm adhesions to the diaphragm and atypical peritoneal folds and attachments, which may be vascular; also aberrant vessels may be present and enter the spleen above or below the hilum. These features vary a great deal. A large adherent friable spleen may render the operation extremely difficult and dangerous, whereas a small non-adherent movable spleen can always be removed without embarrassment.

General anesthesia, usually nitrous oxid ether sequence, is the rule; yet the operation may be performed under nitrous oxid; and Kanavel has demonstrated the possibility of splenectomy under local anesthesia. His patient, suffering from cirrhosis, was in such poor condition as to preclude general anesthesia. The operation was successfully performed under local anesthesia by Labat's method.

The incision must be carefully planned in each case to meet the individual indications. Satisfactory exposure for the removal of a spleen of moderate size is obtained by a high left rectus incision, as this lies approximately over the pedicle, gives ready access to it and allows the delivery of the spleen when freed. The incision is placed about the middle of the left rectus; its length must be planned in accordance with the size of the organ. It may be straight or its ends curved. The Bevan modification is usually satisfactory and is recommended by Balfour (Fig. 64). This incision has the disadvantage that such extensive

abdominal exploration as is often indicated, for instance in pernicious anemia and hemolytic jaundice, is not readily made.

For splenectomy in pernicious anemia, Percy elects a high midline incision so as to explore the rest of the abdominal cavity. He also thinks it is easier to reach the spleen through a midline incision when the pedicle is short. W. J. Mayo has recently expressed a preference for this incision.

A large number of other incisions have been recommended and employed. It has recently been stated that there are twenty-eight methods. These include: vertical incision at outer edge of rectus; transverse incisions; incision along costal arch from ensiform to posterior axillary line; incision beneath the costal arch from rectus to tip of eleventh rib and thence downward; triangular flap by median epigastric incision combined with incision along left costal arch or by median incision with transverse incision to left at its lower end.

For the removal of a very large spleen with dense adhesions, a  shaped combination of vertical and transverse incisions (Fig. 65) may be employed advantageously. The preliminary incision is made from the costal arch to the rectus, parallel to the nerves; it is continued across the left rectus about half way between the umbilicus and xiphoid and thence downward along the mesial border of the rectus to below the umbilicus. If further space is needed, the lower end of the incision is carried across the right rectus. Such an incision was employed recently in the removal of a large spleen of the Gaucher type. The exposure was admirable; the repair of the wound was thoroughly satisfactory. In spite of the transverse rectus division, the abdominal muscles have not been weakened by a normal delivery of a full-term child ten months after the operation.

In order to obtain free access so that firm adhesions to the diaphragm may be more safely divided, Willy Meyer, 1906, employed an osteoplastic flap of the lower cartilages in the removal of a sarcoma of the spleen.

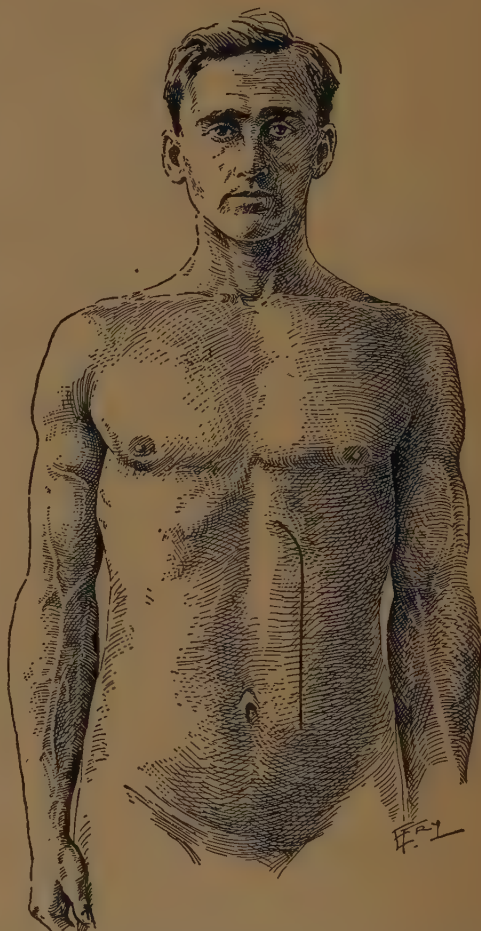


FIG. 64.—BEVAN INCISION AS ADAPTED FOR SPLENECTOMY. (Courtesy of D. C. Balfour, S. G. & O.)

This was done by extending the vertical rectus incision upward, stripping up the thoracic muscles, dividing the lower costal cartilages and turning up the flap. Doyen recommended a similar exposure. Such methods, however, cause undue traumatism.

After the abdomen has been opened, exploration should be made to whatever extent seems appropriate. This feature has been discussed under the consideration of the various conditions for which splenectomy is indicated. The characteristics of the liver, however, should always

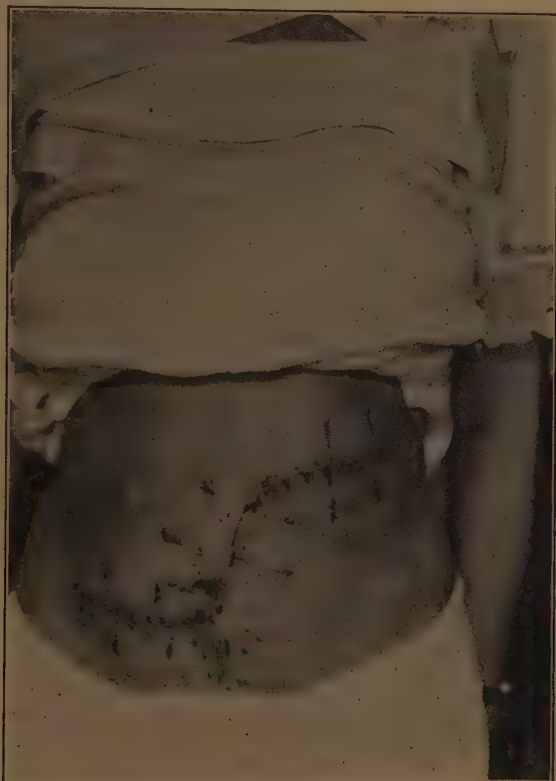


FIG. 65.—SCAR OF WOUND FOR REMOVAL OF LARGE GAUCHER SPLEEN.

Patient has passed through normal pregnancy and labor without weakening the abdominal wall.

be noted. The fixity or freedom of the spleen should then be determined by palpation.

The removal of the spleen may be accomplished by one of two methods: (1) the delivery of the organ first and ligation of its pedicle afterwards; this is the method of choice; or (2) ligation of the pedicle with the spleen *in situ*, freeing adhesions and delivering the organ secondarily. This method is appropriate for cases presenting dense adhesions and friable spleen. Uncontrollable hemorrhage is less likely to occur, since the vessels are controlled before adhesions are freed, but access to the



FIG. 66.—POSITION OF THE GAUZE PACK. (Courtesy of D. C. Balfour, S. G. & O.)



FIG. 67.—RELATIONS OF PEDICLE OF SPLEEN.

pedicle is more difficult and the tail of the pancreas is more likely to be injured.

The first method will be described in detail. It is advocated and employed by most operators, notably Balfour.

Adhesions to the diaphragm are separated manually by gentle manipulation. If they are dense and it can be done, they are ligated, since they often contain vessels. If not ligated, bleeding is controlled temporarily by a gauze pack. Abnormal bands and adhesions are often met with extending from the spleen to adjacent structures, as omentum and colon.

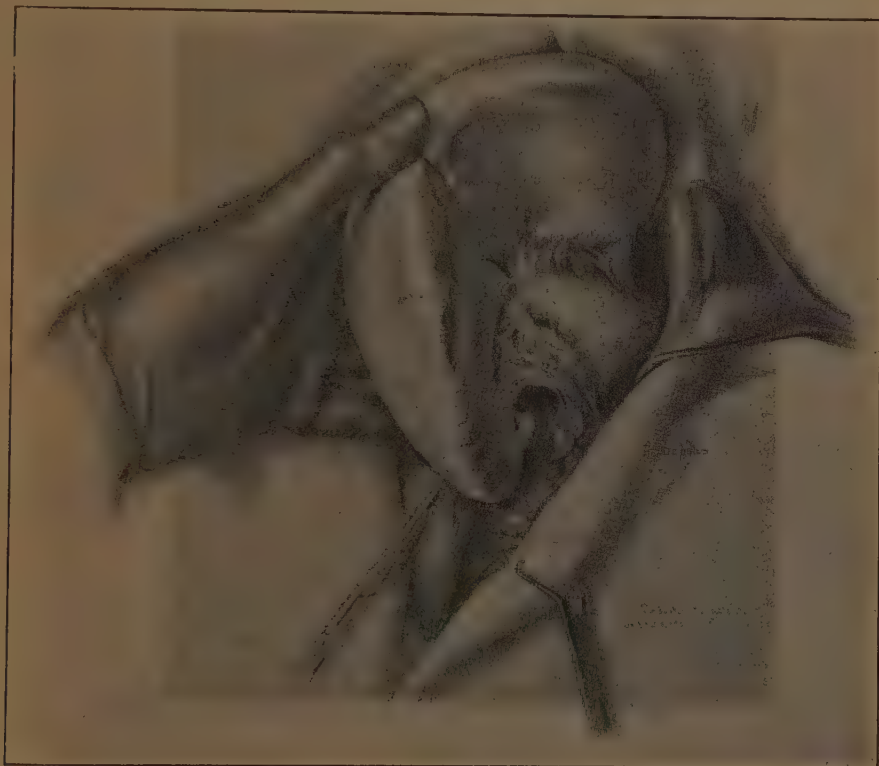


FIG. 68.—POSTERIOR SURFACE OF SPLEEN EXPOSED. (Courtesy of D. C. Balfour, S. G. & O.)

This shows tail of pancreas which lies in the splenic pedicle, posterior to vessels. The pancreas should be dissected from its position before clamps or ligatures are applied.

These may be firm and contain vessels and must be divided between ligatures. It is also advisable to divide the gastrosplenic omentum between ligatures near the spleen. The spleen should now be sufficiently free to be delivered, which should be done gently without great traction, the lower pole first. As the spleen is lifted from its bed, a hot gauze pack is placed under pressure behind it and left until the spleen has been removed. This step was suggested by W. J. Mayo and is of value for the control of hemorrhage. Gentle traction often allows the spleen to be lifted out of the abdomen and the pedicle freely exposed.

The splenic pedicle is sometimes sufficiently long and compact to warrant its ligation *en masse*. But mass ligation is not in general the procedure to be recommended. It is better to identify the vessels and ligate them serially. This step is facilitated if the gastrosplenic omentum has been divided. Moreover, the greater curvature of the stomach, which should always be identified, is thus freed and may be drawn to the right. Otherwise the stomach may be accidentally injured and even opened. The tail of the pancreas must also be recognized and avoided. It is in close relationship with the spleen; even when the spleen is drawn forward, the tail of the pancreas, which lies posterior to the vessels, may remain in contact with the spleen. The pancreas can usually be protected by slight pressure mesially between finger and thumb. But a closely lying tail must be separated by dissection. Balfour turns the spleen to

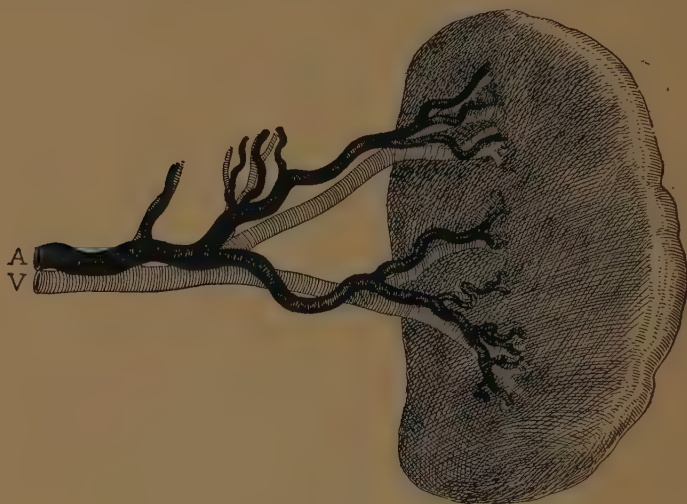


FIG. 69.—RELATION OF VESSELS AT HILUM.

the right so that its posterior surface is exposed, showing the tail of the pancreas. The pancreas can thus be more easily freed.

Having displaced the stomach and safeguarded the pancreas, the vessels are ligated. Their relationship and position vary a great deal. In Fig. 69 is shown what may be considered a classical arrangement. The vessels are spread out like a fan. Frequently, however, they are more closely bunched into a shorter hilum and present fewer branches. The veins are large and friable and, if torn, are the source of severe hemorrhage; they have no constant relation to the arteries. Various methods may be employed to secure the pedicle and no arbitrary rule can be followed. With aneurysm needle catgut ligatures may be passed through the pedicle and the vessels ligated serially in two or more groups. A clamp is then placed across the pedicle close to the spleen to prevent annoying hemorrhage from the organ; the pedicle is divided and the spleen removed. If there is any uncertainty as to the placing of or

security of the ligatures, a light curved stomach clamp with blades protected by rubber tubing may be placed proximal to the line of ligatures.

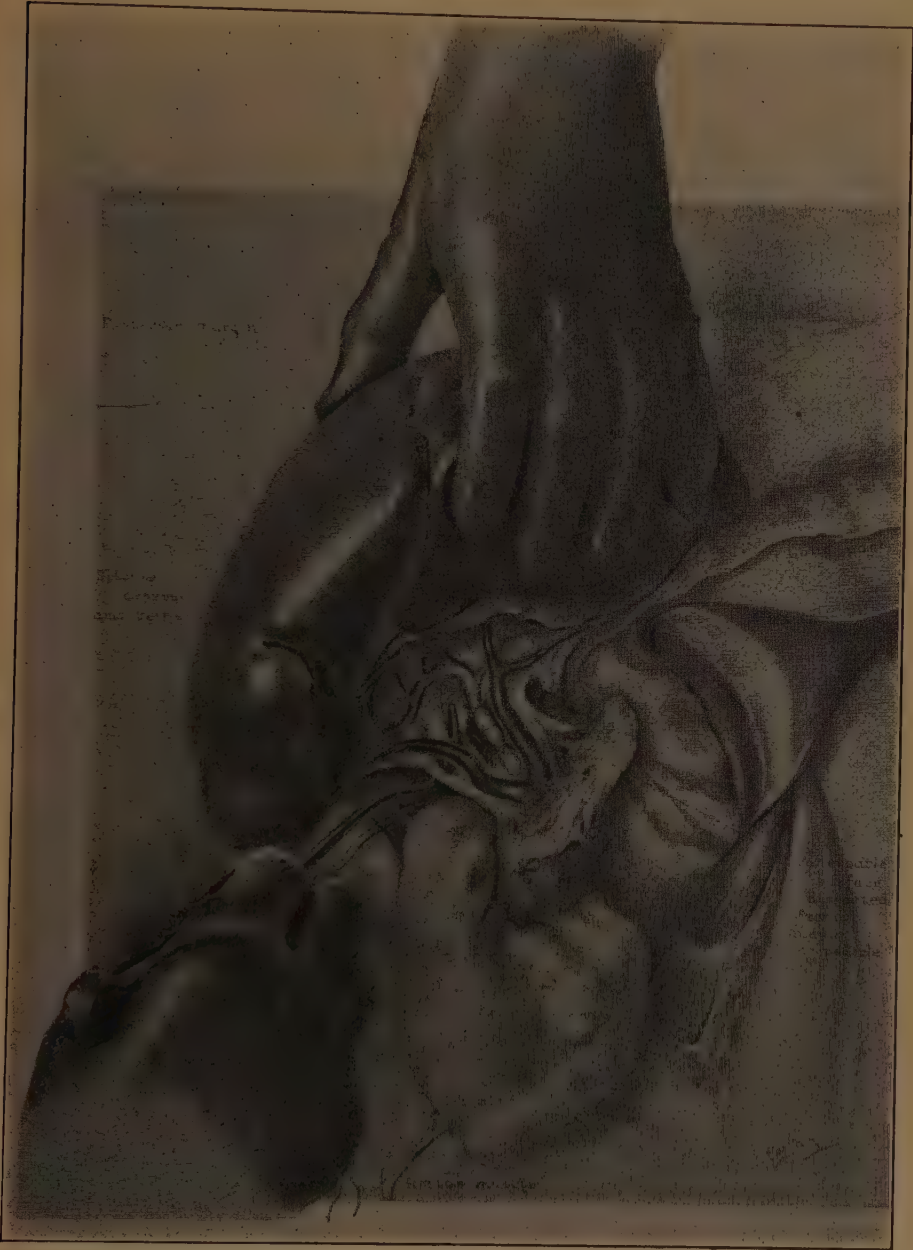


FIG. 70.—LIGATION OF SPLENIC PEDICLE. (Courtesy of D. C. Balfour, S. G. & O.)

This will prevent retraction of unsecured vessels and will control hemorrhage until such vessels can be secured. It must be emphasized that in passing a needle through the pedicle a point between the vessels should

be carefully selected, otherwise a vein may be torn and annoying hemorrhage result. Instead of ligatures, clamps may be employed. Mayo suggests the use of three clamps. When the pedicle is divided, one clamp prevents a flow of blood from the spleen and two are left on the pedicle. Ligatures are tied first in the groove of the deeper clamp, and second in the groove of the superficial. To diminish the amount of blood



FIG. 71.—PERITONEAL ATTACHMENTS SEPARATED, MOBILIZING SPLEEN AND PERMITTING APPLICATION OF CLAMPS. (Courtesy of D. C. Balfour, S. G. & O.)
Pedicle to be divided at dotted line.

in the spleen, Mayo compresses the splenic artery for a short time prior to clamping the pedicle.

The spleen having been cut away, the gauze pack is removed. All denuded areas should be carefully closed by suture. Mayo described a useful method, the snake suture, for this purpose, covering over the denuded surfaces with a fine needle and gut. Absolute hemostasis should be secured and the wound closed without drainage.

Alternative Method.—This may be employed in cases where dense adhesions are encountered between the diaphragm and the spleen. Under such conditions hemorrhage is less if the pedicle has been ligated; moreover, such bleeding as occurs may be more readily controlled if the spleen can be removed soon after hemorrhage begins. The adhesions between the spleen and diaphragm are not separated primarily. The anterior

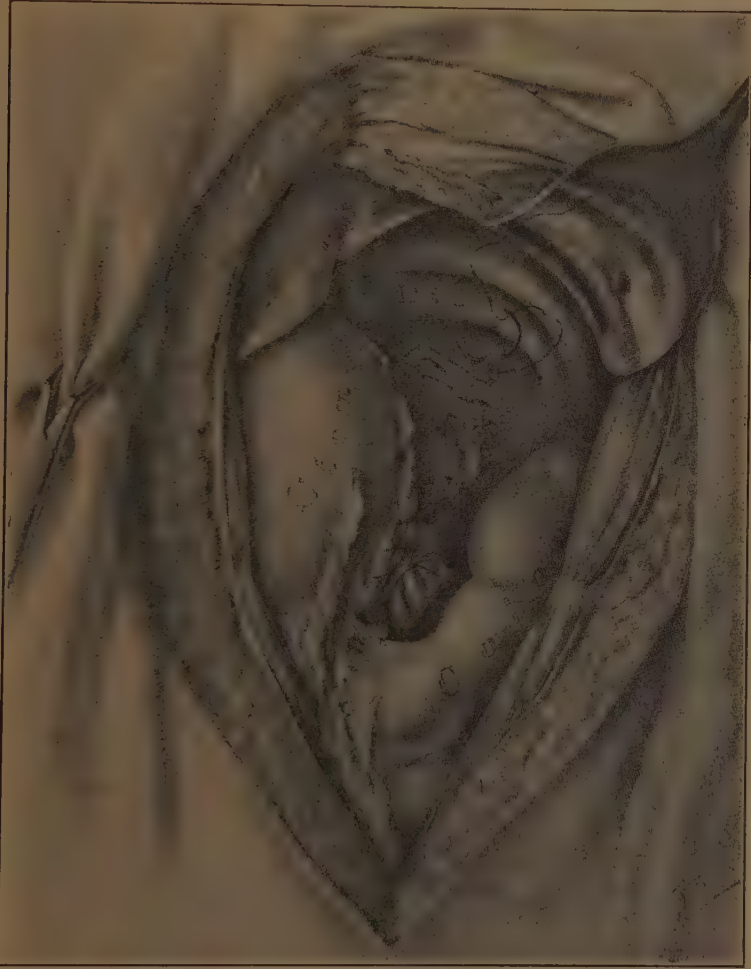


FIG. 72.—CLOSURE OF SPLENIC SPACE BY SNAKING CATGUT SUTURE, TO CONTROL OOZING OF BLOOD FROM DEEP-SEATED AREAS. (Courtesy of W. J. Mayo, *Annals of Surgery*.)

edge of the spleen is displaced outward so as to expose the region of the hilum. The gastrosplenic omentum is opened between ligatures so as to expose the pedicle. A finger is slipped beneath the pedicle and the tail of the pancreas is drawn mesially. The vessels of the pedicle are ligated serially. If possible, they should be ligated doubly; one ligature, close to the spleen; the other, about an inch distant and vessels divided between. The adhesions are then freed and the spleen removed. In

this procedure, it must be recognized that the spleen *in situ* falls somewhat to the right, and the tail of the pancreas, if long, buckles so as to lie with its anterior surface against the hilum and even the gastric surface. This renders the relationship much closer than prevails when the spleen is dislocated and drawn forward as in the first method.

In very large spleens, when a  shaped incision is used, the lower pole may be delivered and the pedicle ligated from below upward, leaving the adhesions at the upper pole until the pedicle has been divided. These adhesions are then clamped and divided and the spleen removed at once. There is likely to be less bleeding by this method.

In very difficult adherent cases, Lombard recommends decortication of the spleen. The plane of cleavage lies between the thickened capsule and the splenic tissue. The capsule is incised and the fingers inserted between it and the spleen, which is decorticated and freed. As a preliminary, the pedicle is ligated or compressed with clamps. By this method, Lombard states that he removed a spleen with no hemorrhage. The method, however, does not commend itself.

Because the arterial supply of the spleen is more accessible at certain points than the deeply situated pedicle of the organ, Gerster believes that a difficult splenectomy can be facilitated by means of temporary or permanent ligation of the splenic and left gastro-epiploic artery. The splenic artery is exposed close to the celiac axis through openings in the lesser omentum and the posterior parietal peritoneum. On account of the free anastomosis between the left and right gastro-epiploic arteries, the former should be tied where it reaches the stomach wall, just before branches are given off from it to the anterior and posterior surfaces. Ligation of the vasa brevia is rarely called for. Gerster states that the loss of blood incident to excision of the spleen is greatly diminished by this method. The procedure, however, does not seem necessary.

Postoperative Complications Following Splenectomy.—*Collapse* and *shock* have been attributed to forcible traction on the splenic pedicle, resulting in irritation of the solar plexus. The sympathetic fibers undoubtedly play a part in these cases, in addition to the loss of blood or the length of a difficult splenectomy. Gentleness is, therefore, strongly indicated as in all operations involving the upper abdomen.

Hemorrhage may occur in the course of the operation or during the hours following it and constitutes the most dangerous complication of the surgery of the spleen. It may be due to the peculiar friability of the organ; the great difficulty of freeing a firmly adherent spleen; the slipping of a ligature. Careful technic minimizes this danger, while the hemorrhagic tendency which often prevails in these patients is to some extent controllable by transfusions of blood.

Pneumothorax occasionally results from a tear in the diaphragm during the separation of an adherent spleen. We have seen one such accident, and other cases have been reported. Such an opening should be repaired by suture.

Pneumonia is a relatively frequent complication.

Portal thrombosis is an occasional and serious complication of splenectomy. We have learned of a few cases through personal communications, but reports of such cases have been infrequent. In 1911, Prudnikon operated upon a woman forty-six years of age, who died on the eleventh day after splenectomy for movable spleen. Repair of an abdominal hernia was done at the same operation. Autopsy showed thrombosis which began in the splenic vein and extended into the portal vein and the veins of the liver. Infection was absent and the venous thrombosis was explained by the observer as due to increased coagulability of the blood.

Injury to the Pancreas.—Elevation of temperature which cannot be explained by infection or other complication has been mentioned as occurring during convalescence after extirpation of the spleen. Herczel has given this feature considerable study. Among the 5 cured cases of splenectomy quoted by this author, fever was observed 3 times. He was convinced that the fever was referable to fat necrosis in the retroperitoneal tissues caused by injury to the pancreas. In his last 2 cases, he preserved the pancreatic tissue by ligating the splenic vessels individually close to the hilum. In these 2 cases, fever did not occur. Upon the basis of these cases, Herczel recommends that clamps be discarded and no mass ligatures be applied.

Herczel emphasizes that the elevations of temperature after extirpation of the spleen show remissions, or even intermissions. He further states that after the fever has subsided symptoms of serious infection may develop due to late bacterial growth in the necrotic tissues. It cannot be too strongly urged that the pancreas should be carefully avoided in clamping or ligating the pedicle. Fontoynt ligated the tail of the pancreas with resulting necrosis of the neighboring peritoneum. If it is recognized that the tail of the pancreas has been injured, a drain should be introduced to this region.

Injuries to the stomach are rare. Balfour reports a case in which the stomach was opened but immediately repaired and no postoperative complications ensued.

Splenotomy.—Splenotomy (incision of the spleen) is indicated in some cases of abscess of the spleen and in suppurating cysts. The avenue of access varies according to the requirements of the case. It may be subcostal, transcotal, or transpleural and may be performed in one or two stages. (*cf.* Abscess, Tuberculosis and Cysts.)

Splenorrhaphy.—Splenorrhaphy consists in suture of wounds of the spleen, and, although theoretically an ideal procedure, as it permits the preservation of the organ, hemostasis is not reliable. It is, therefore, employed exceptionally and only in small wounds (*cf.* Wounds of Spleen). The first successful splenorrhaphies were probably performed by Parlavecchio, in 1893, and Impallomeni, in 1894.

Ligature of the Splenic Pedicle.—This was advocated by Clément Lucas, in 1882, with the object of causing atrophy of an enlarged spleen, especially in cases complicated by extensive adhesions. It has been

performed occasionally for rupture of the spleen. The procedure, however, is unwarranted on account of the danger of necrosis of the organ. The rare cases of ligation of the splenic artery were formerly invariably followed by death, but the operation was performed with a successful outcome by Lanz, Amsterdam, 1914, in the case of a man twenty-four years of age. The spleen was displaced and caused severe abdominal pain, especially on urination. A round movable swelling of firm elastic consistence the size of a fist, which could be felt in the left hypogastric region, was found to drop into the pelvis on emptying the bladder with the catheter, and to ascend again when the bladder was filled with a solution. Median laparotomy showed a displaced spleen which was broadly adherent to the posterior vesical wall. The veins of the splenic pedicle were enormously dilated and tortuous. Splenectomy did not appear advisable on account of the close splenovesical adhesions. Therefore ligation of the splenic artery was made. Recovery was uneventful; six months later no trace of the mass was demonstrable and the patient was free from all disturbances.

Stubenrauch ligated the main trunk of the splenic artery, at a distance of 8 cm. from the spleen, in a man sixty-six years of age, who suffered from recurrent cutaneous hemorrhages, as well as renal and intestinal hemorrhages. The patient was enabled to resume his clerical work, and remained free from hemorrhages or other disturbances. Upon the basis of this case, and other reports in the literature, Stubenrauch recommends ligation of the splenic artery instead of extirpation of the spleen in certain blood diseases. He states that necrosis of the spleen can be avoided if care is taken not to injure the splenic vein and the ligature is applied at a sufficient distance from the hilum of the spleen to preserve the anastomosis between the splenic artery and the left gastro-epiploic artery.

In the discussion of Stubenrauch's report, v. Haberer pointed out, on the basis of 3 cases of gastric resection, in which the splenic artery had to be tied, without subsequent damage to the spleen, that the ligation of this vessel is harmless, provided the ligature is applied proximal to the short gastric arteries. Necrosis of the spleen will not follow under these conditions, but does occur when the ligature is applied close to the hilum.

Splenopexy.—Splenopexy consists in the fixation of a movable spleen. It was first performed by Tuffier, in 1882. The methods which have been employed are intraperitoneal fixation, extraperitoneal fixation and combined intraperitoneal and extraperitoneal fixation. These operations are rarely, if ever, performed; therefore a very brief outline of the procedures is sufficient.

According to Rydygiel's method, the under surface of the diaphragm is exposed, and a transverse incision on the level of the ninth or tenth rib is made through the peritoneum which is separated with the finger so as to form a pocket. Sutures are placed around the margins of the pocket to limit the cavity into which the spleen is then placed.

Kouwer employed tampons to fix the spleen and favor the development of firm adhesions between the spleen and diaphragm.

Greifenhagen fixed the spleen by sutures. This procedure consists in passing silk sutures through the muscular layers and peritoneum on one side of the abdominal wound, through the spleen, and then through the peritoneum and the muscular layers on the opposite side. The threads are tied after closure of the peritoneal wound.

Tuffier also sutured the spleen to the diaphragm or abdominal wall. Such methods obviously expose to the danger of serious hemorrhage (Moynihan).

Bardenheuer's method displaces the spleen into the extraperitoneal tissues. A vertical incision in the axillary line is made from the tenth rib downward. The peritoneum is exposed and separated over a wide area. It is then opened sufficiently to allow the delivery of the spleen, which is placed in the extraperitoneal pocket.

Basil Hall, in the case of a woman thirty years of age with a wandering spleen, found after delivery of the organ through an abdominal incision, that an extremely deep notch on the anterior border two to three inches from the lower extremity of the spleen could be utilized to fix the organ. The main body of the spleen was replaced in the abdomen. Then, while the lower pole was held in the wound, the edges of the peritoneum were drawn tightly by a purse-string suture so as to grip the narrow isthmus in the notch. The abdominal aponeurosis was sutured in a similar manner. The patient made a good recovery and was entirely relieved of her symptoms.

Exosplenopexy, or suturing the spleen, in an opening in the abdominal wall has occasionally been performed. The first attempt of this kind was made by Jaboulay, in 1893.

In the performance of exosplenopexy, the projecting spleen has either been surrounded by gauze interposed between it and the borders of the incision, with the object of favoring adhesions, or the spleen has been sutured to the wound margins. Houzel, in 1897, performed this operation in a case of enormously enlarged and extensively adherent spleen, which had been mistaken for ovarian cyst, and the patient made an excellent recovery. In a case of tuberculosis of the spleen, reported by Quénu and Baudet, in which splenectomy was impracticable on account of extensive adhesions, the enlarged organ was attached to the parietal peritoneum and incised; the spleen sloughed off some days later and the patient recovered.

Resection.—In some rare cases of nonparasitic cysts, benign tumors, etc., especially if situated in the lower pole of the spleen, resection has been successfully accomplished. The excision should be wedge-shaped so that the raw surfaces may be closely approximated by sutures, taking broad bites of splenic substance.

Two additional interventions which have been recommended in the

treatment of certain diseased conditions involving the spleen are splenocleisis and omentopexy.

Schiassi's operation, done in part for the purpose of splenocleisis, aims at the production of a large connective tissue capsule surrounding the spleen and furnishing new vascular relations to the organ, the object being to lessen the passive congestion of the spleen and to improve the circulation of its interior. As a cure for ascites, Talma suggested the establishment of vascular anastomoses between the deep circulation of the abdomen and that of the abdominal wall. A procedure derived from Talma's operation was described by Schiassi with the object of sidetracking some of the blood of the portal system. It consists essentially in spreading the great omentum over the parietal peritoneum, under a flap composed of fascia and muscles (omentopexy). This procedure seems to have been successfully combined with splenectomy in a few cases of Banti's disease with profuse ascites.

Transplantation of the spleen has not been attempted in the human subject, since the loss of the organ occasions no disturbance. But autoplasmic and homoplasmic transplantations of the spleen have been attempted in animal experiments on dogs by Konamura (1919). The spleen was divided into two parts and the portion with the best blood supply was implanted in the abdominal cavity, in the neck or grafted into the renal vessels after nephrectomy. The transplanted organ promptly underwent necrotic changes or became absorbed.

Transplantations have frequently been made into the spleen on account of the high vascularity of that organ. The thyroid and parathyroid glands have been implanted by many investigators in animals. Payr and Kotzenberg have made such implantations for myxedema. In both cases improvement was reported. Pratt and Murphy have employed the spleen experimentally for the implantation of pancreatic tissue.

Transfusion.—Transfusion plays an important part in the surgery of the spleen. Its indications have been discussed under the separate diseases and blood grouping has been considered in Chapter IV. In a considerable proportion of the cases in which splenectomy is indicated, the blood picture is that of profound anemia. Without transfusion, many of the cases operated upon successfully in recent years would doubtless have died as the result of the operation. The indications for transfusion are ante-operative anemia, operative hemorrhage and shock. In cases showing a moderate degree of secondary anemia, a transfusion may be performed to advantage shortly before the operation; Frazier advises it forty-eight hours prior to operation for hemoglobin under 40 per cent. The time element does not appear of great importance and we have found good results from transfusion immediately before operation, as in a case described under splenic anemia. In severe secondary anemia, however, a test transfusion should be given several days before the contemplated operation, the purpose being to note the

reaction of the patient to the transfusion. Occasionally the benefit is entirely transitory. In that case, the response is likely to be no better if another transfusion is given either during or after the operation. Minot considers that the best results are obtained by transfusion about four days before operation. If the case responds well to the preliminary transfusion, preparations should be made for a second transfusion soon after the operation, if this should be necessary.

In pernicious anemia, transfusion plays an especially important rôle. The treatment of the disease consists in three main factors: (1) repeated transfusions of blood; (2) removal of foci of infection; and (3) splenectomy.

The amount of blood transfused varies with different operators from 200 c.c. to 800 c.c. repeated at from seven to fifteen-day intervals. The patients usually improve as a result of the transfusions, so that splenectomy can be done without undue danger.

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